MORBID OBESITY AND HEALTH RELATED QUALITY OF LIFE

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CONTENTS

List of papers:

Paper I. Lund RS, Karlsen TI, Hofsø D, Fredheim JM, Røislien J, Sandbu R, Hjelmesæth J. Employment is associated with the health-related quality of life of morbidly obese persons. Obes Surg. 2011;21:1704–1709
DOI 10.1007/s11695-010-0289-

Paper II. Karlsen TI, Lund RS, Røislien J, Tonstad S, Natvig GK, Sandbu R, Hjelmesæth J. Health related quality of life after gastric bypass or intensive lifestyle intervention: a controlled clinical study. Health Qual Life Outcomes. 2013;11(1):17.
DOI 10.1186/1477-7525-11-1723406190

Paper III. Karlsen TI, Tveitå EK, Natvig GK, Tonstad S, Hjelmesæth J. Validity of the SF-36 in patients with morbid obesity. Obes Facts 2011;4:346-351.
DOI 10.1159/000333406

Abbreviations

ACSM	American College of Sports Medicine
ADL	Activities of daily living
AHI	Apnoea-hypopnoea Index
AMOS	Statistical software package for structural equation modelling
ANCOVA	Analysis of covariance
BED	Binge eating disorder
BMI	Body mass index
BN	Bulimia nervosa
CFA	Confirmatory factor analysis
CFI	Comparative fit index
CI	Confidence interval
ES	Effect size
FIML	Full information maximum likelihood
GP	General practitioner
HbA1c	Glycosylated haemoglobin A1c
Hg	Mercury
HRQL	Health related quality of life
HUNT	The Nord-Trøndelag health study
ILI	Intensive lifestyle intervention
IWQOL	Impact of weight on quality of life
mm	Millimetres
mmol	Millimole
MOBIL	Morbid obesity treatment, bariatric surgery versus intensive lifestyle intervention
OR	Odds ratio
OSA	Obstructive sleep apnoea
OWLQOL	Obesity and weight loss quality of life
PA	Physical activity
PCA	Principal component analysis
PRELIS	Statistical software package for structural equation modeling
QOL	Quality of life
RMSEA	Root mean squared error of approximation
RYGB	Roux-en-Y gastric bypass
SD	Standard deviation
S_{diff}	Standard error of difference
SE	Standard error
SEM	Standard error of measurement
SF-36	Medical outcomes study Short-Form-36
SOS	Swedish obese subjects
SPSS	Statistical package for the social sciences
WC	Waist circumference
WHO	World Health Organization
WRSM	Weight related symptom measure
$\eta\rho^2$	Partial eta squared
χ^2	Chi square

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1. Introduction

1.1 Classification and prevalence of obesity

The World Health Organization (WHO) defines obesity as a disease in which excessive body fat has accumulated to such an extent that health may be adversely affected [1]. When comparing the prevalence of the disease across cultures, we need a classification and standardized measurements. The Body Mass Index (BMI) [1] is one common measure used to assess the degree of overweight and obesity. BMI is defined as weight in kilograms divided by the square of height in metres (kg/m^2). On the basis of epidemiological studies, the WHO has concluded that a BMI between 18.5 and 25 kg/m^2 is to be considered "normal weight", a BMI between 25 and 30 kg/m^2 is to be considered "overweight", whilst a BMI score $\geq$ 30 kg/m^2 is to be considered "obese" [1]. Morbid obesity is understood as a BMI $\geq$40 kg/m^2 or $\geq$ 35 kg/m^2 with at least one comorbidity [2]. A comorbidity is understood as any condition associated with obesity that usually worsens as the degree of obesity increases and that often improves as the condition is treated [3, 4].

The amount of excess fat, its distribution within the body, and the associated health consequences vary considerably between obese individuals. BMI does not discriminate between weight associated with muscles and weight associated with fat mass, nor with the fat distribution within the body. In this sense, well-trained individuals may have scores on the BMI-index indicating overweight or even obesity without having an abnormal or excessive body-fat accumulation. The WHO has outlined some of the other weaknesses associated with BMI measurements [1, 5], drawing specific attention to the fact that BMI may not correspond to the same percentage of body-fat across populations. Even with an identical BMI, Polynesians tend to have a lower percentage of body-fat than Caucasian Australians [6]. The percentage of body-fat, especially abdominal fat, also tends to increase with age in both sexes

[7], and is generally higher in women than in men [8]. In spite of these weaknesses, the WHO has proposed using BMI for epidemiological research in order to measure the potential health hazardous fat accumulation in individuals [1, 5]

The WHO has declared that the incidence of obesity has reached epidemic proportions [1], and a 2011 meta-analysis published in *The Lancet* reported nearly a doubling of obesity worldwide as measured by BMI: approximately 5% (men) and 8% (women) in 1980 to 10% (men) and 14% (women) in 2008 [9].

The prevalence of obesity in Norway has tripled between 1960 and 2000 [10]. A number of Norwegian studies have provided epidemiological data; the Nord-Trøndelag Health Study ("Helseundersøkelsene i Nord-Trøndelag", HUNT) consists of three surveys (1984-86, 1995-97 and 2006-08). The three surveys show how obesity increased from approximately 14% to 19% to 23% in women, and from 8 % to 14% to 22% in men. The prevalence of extreme obesity (BMI $\geq$ 40 kg/m^2) was .5% in men and 1.5% in women (2006-2008) [11]. This development is similar to that of other countries, but not as far-reaching as in the USA. In the USA the prevalence of obesity in 1999-2000 (as measured by BMI) was 28% (men) and 33% (women). In 2009-2010 the prevalence had raised to 36% in both men and women. The prevalence of extreme obesity (BMI $\geq$ 40 kg/m^2) in the USA was 4% in men and 8% women (2009-2010) [12].

There is comprehensive evidence that *abdominal* adiposity represents an increased risk of illness and premature death [5, 13, 14]. Abdominal adiposity refers to a large proportion of fat mass situated around the intestines and in the liver. On the basis of such evidence the WHO proposes that measurements of waist circumference (WC) be applied as a primary individual measure of overweight and obesity. As with BMI, there are cut-off values relating to the level of health risk. Utilising a Dutch study [15] of 2183 men and 2698 women aged

20-59 years, the WHO proposes a WC of 94 cm and 102 cm for Caucasian men, and a WC of 80 cm and 88 cm in women. These figures are thresholds for increased or substantially increased risk of metabolic complications associated with obesity [5].

The increase of WC in Norway is alarming. The HUNT study [11] found that mean (SD) WC among women increased from 81.4 (11.4) to 90.3 (12.7) cm in HUNT 2 (1995-97) and HUNT 3 (2006-08). The corresponding WC increase amongst men was 91.9 (9.3) to 97.4 (10.5) cm. In HUNT 3, *abdominal obesity* (WC ≥ 102 cm in men and 88 cm in women), which indicates a substantially increased risk of metabolic consequences, was found in 56% of women compared to 32% of men. The findings from the HUNT 3 study indicate that severe obesity has also become a concerning health issue in a Norwegian context [11].

1.2 Causes of obesity

The academic literature points to many different explanations for this epidemic of obesity. Some diseases and syndromes may cause obesity, whilst we know that certain medicines, such as psychotropic drugs [16] and oral contraceptives [17], are associated with weight gain. Genes do play a role [18, 19]. Genes regulate the capture, storage and release of energy from food and this genetic function is a prerequisite for our survival, both as individuals but also of humans as a species. Our genetic regulatory system seems to be designed to create fat storages to be used as energy depots in times of food scarcity. For most people, in environments with a food surplus, our genetic mechanisms do not seem to have the same appropriate regulatory functions; the genetic system does not impose fat reduction – only the opposite. The variance between different individuals in terms of their susceptibility to weight gain may be explained by a gene-environment interaction [20]. This refers to a situation where the effect of an individual's behaviour on weight gain is influenced or modified by the individual's genetic composition [20]. However, the genetic composition of the population

does not change rapidly. The large increase in the prevalence of obesity during the last few decades must thus reflect changes in other factors than human genetics [19].

The most prominent environmental explanations accounting for the increased prevalence of obesity are related to an efficient food energy supply increasing the energy intake, combined with a decrease in physical activity related to more effective means of transportation and the mechanisation of working life [19]. In the literature the use of "obesogenic environment" has become commonplace. An obesogenic environment represents the *created* general working and living conditions which promote excessive food-intake and demotivate individuals from engaging in physical activity [21]. Reduced physical activity and changes in the global food system, including reductions in the time-cost of food, seem to be the major drivers of the rise of the global obesity epidemic [19]. Other factors (sleep debt, endocrine disruptors, reduction in variability of ambient temperature, decreased smoking, changes in distribution of ethnicity and age, higher age at first pregnancy, epigenetics, and natural selection of obesity specific genotypes) have been discussed as additional explanations to the obesogenic factor [22, 23].

1.3 Consequences of obesity

The link between obesity and disease was first acknowledged by the ancient Greeks, with Hippocrates as a forefather also in this perspective [24]. Following the increased prevalence of obesity, the volume of research on obesity's consequences has grown rapidly over the past few decades. It is now widely recognised that obesity, and especially abdominal adiposity [13, 14], is a major contributing factor in the development of chronic diseases like type 2 diabetes mellitus, hypertension, obstructive sleep apnoea, cancer, heart and vascular diseases, gallbladder disease as well as a number of other disorders [4, 25-28]. Morbid obesity is also associated with higher mortality [29, 30], increased psychological distress [31-36] and impaired quality of life [32, 37-45].

1.3.1 Quality of life

Quality of Life (QOL) is a broad concept and refers to how well an individual functions in daily life and his or hers perceived well-being [46]. The concept can be related to many areas of life, with most people having an intuitive understanding of their personal QOL in regard to such areas.

The definition of QOL varies. WHO has defined *health* as a state of complete physical, mental and social well-being, and not merely the absence of disease or illness [47]. The multidimensionality of health is noteworthy, and a WHO work group has identified the following cross-cultural elements to QOL: physical health, mental health, social relationships, environment, as well as overall QOL [48].

To distinguish between the general concept of QOL in clinical and health research the term health-related quality of life (HRQL) is frequently used [49]. The most common understanding of HRQL is that it is a multidimensional measurement of the impact an illness and/or its treatment has on individuals [50, 51]. To clinicians, researchers and scholars occupied with problems relating to health, well-being and illness, HRQL is of special interest as it reflects an individual's subjective response and assessment of his or her state of health. The multidimensionality of the concept opens for investigations into different areas or dimensions; physical, mental, emotional and social to name only a few [52].

Measurement of quality of life

While studies of QOL and HRQL can be performed using qualitative research methods [53], measurements of HRQL are largely quantitative and achieved through standardized questionnaires (instruments) which assess the different aspects of HRQL.

There are two basic approaches to quantitative HRQL assessments [37]. The first involves the use of instruments that measure broad and generalized aspects of HRQL (generic instruments). The second approach to HRQL assessment involves the use of instruments that are specific to a disease (eg. obesity), population (eg. adolescents or adults), and/or clinical problem (eg. sexual function, pain).

Different instruments have been developed in defined cultural settings with samples representing specific populations. When selecting an instrument for research purposes, it is important that the instrument is validated for use in the culture and population in question, as well as for the clinical problem it is intended to be used in.

Generic instruments

The main advantage of generic instruments is that they allow comparisons both between diagnostic groups as well as between diagnostic groups and the general population. The main drawback with generic measures is that it is not possible to determine if respondents attribute their HRQL to their specific disease (eg. obesity) or to other factors (eg. age or a comorbid condition such as diabetes). There are many generic instruments, though the most commonly used in health (and societal) research is the Medical Outcomes Study Short-Form-36 (SF-36) (appendix 1).

SF-36 is based on 36 items [54-56]. Item 2 is not included in the scoring of the instrument [56] and is a question on health change over the last 12 months. The remaining 35 items are

scored into eight domains (physical function, role physical, bodily pain, general health, role emotional, social function, vitality, and mental health) which can be combined into two summary scores; the physical and mental dimensions [57]. The scoring and calculations are standardized by the scale authors [57]. There has been raised criticism on the scoring of the two main dimensions [58, 59] [58-60] on which type of factor score that should be applied and different alternatives have been suggested [61].

The SF-36 was developed in conjunction with the 1988-89 US Medical Outcomes Study [62]. Outcomes included end points such as physical, social, and role functioning in everyday life, and patients' perceptions of their general health and well-being and satisfaction with their treatment. Adult patients (n = 22,462) evaluated their health status and treatment. A sample of these patients (n = 2,349) with diabetes, hypertension, coronary heart disease, and/or depression were selected for further longitudinal studies and formed the basis for the development of the instrument [54]. Thereafter the instrument has become the most widely used generic HRQL instrument, and according to the website of the SF-36 stakeholders [63] it has been documented in more than 4000 publications. The instrument has been validated for many diagnostic groups and translated into more than 22 languages.

The validity of the instrument in a morbidly obese population has not been properly tested, but a 2006 Italian observational multicentre validation study of 1735 obese outpatients of whom 60% had a BMI $\geq$ 35 kg/m^2 raises some questions [64]. A principal component analysis (PCA) with an oblique rotation suggested a 6-component solution instead of the original 8-component solution, thereby questioning the construct validity of the 8 SF-36 subscales in patients with obesity. The study found a peculiar clustering of some SF-36 items and their relationship with BMI, suggesting that the HRQL profile of subjects belonging to

that population may be better described with alternative aggregations of the SF-36 items or with disease-tailored questionnaires. The study did not assess the structural validity of the two summary scales [64].

Disease-specific instruments

Disease-specific instruments contain questions (items) that reflect the most relevant characteristics or problems connected to a specific disease or condition. There are several obesity specific HRQL-instruments [52, 65]. Examples of well-designed and validated weight-specific HRQL measures are the Obesity and Weight Loss Quality of Life Questionnaire (OWLQOL) (appendix 2) and the Weight-Related Symptom Measure (WRSM) (appendix 3) [66, 67].

The OWLQOL questionnaire is developed by the University of Washington between the years 2000 and 2004 [66, 67]. The scale authors used a theoretical model for perceived HRQL to identify and select items that assessed emotional feelings in persons with obesity [52, 65].

The instrument consists of 17 statements about weight-related feelings and emotions which are rated on a seven-point scale that ranges from 0 ("not at all") to 6 ("very large"). The 17 items of the OWLQOL form a scale ranging from 0-102, with higher scores indicating a better emotional HRQL.

Validation studies of the OWLQOL have been performed in the US, Italy and France (n = 6,107). Mean BMI in these three studies varied from 33-37 kg/m^2, whilst age varied from 45-51 years and the proportion of females from 40-82%. The studies concluded that the instrument were brief, valid, reproducible and responsive on measurement of self-reported outcomes in obesity [67].

The WRSM questionnaire was produced in conjunction with the OWLQOL and was validated in the same studies reported above [66, 67]. The instrument measures twenty obesity specific symptoms using two different sets of items.

The first set of items assesses whether or not the patient is experiencing specific symptoms. The scoring of this set of items creates an additive scale summing up the number of symptoms, ranging from 0–20. The second set of items concerns the distress symptoms impose, with values from 0 (“not at all “) to 6 (“very large“). They form a symptom distress scale ranging from 0–120, where higher scores indicate worse symptom distress.

1.3.2 Physical functioning and HRQL in morbid obesity

Impaired physical functioning in morbidly obese persons is most likely caused by continuous increased strain on the musculoskeletal, respiratory and cardiovascular systems. Obesity, and especially abdominal adiposity, is associated with increased pressure on organs due to fat mass, making breathing difficult and decreasing the flexibility of body movements. However, the metabolic effects of obesity may also have a have an additional degenerative effect on the development of comorbidities and musculoskeletal pain [68].

A Swedish study (n = 5,633) applying the SF-36 reported that overweight and obesity in young (16-34 years) men and women had a largely negative effect on physical health. Among the middle-aged (35-64 years), obese women reported more physical HRQL-impairments [mean (SE) 79 (2) points] than obese men [mean (SE) 87 (1) points] [38]. This finding is consistent with the findings of a study review which explored the influence of obesity on HRQL. The authors concluded that obesity-associated detrimental effects on HRQL tend to be most pronounced in physical domains regardless of the applied HRQL-instruments [37].

There is a significant association between increasing BMI and impaired physical HRQL, where individuals with morbid obesity have the lowest scores on physical HRQL [37, 43] and physical functioning measures [69]. Adequate walking capacity and physical stamina are important elements of an individual's physical HRQL, and data based on time to exhaustion while walking on a treadmill have shown that the prevalence of individuals with low cardiorespiratory fitness increases by about 5 % per unit increase of BMI above 25 kg/m^2 [69]. Common physical problems in morbidly obese individuals include doing moderate/vigorous activities, an inability to climb stairs, carrying groceries, walking long distances, trouble bending down, inability to tie shoe laces and difficulty getting up from chairs. These may all affect the activities of daily living (ADL). The physical limitations can be especially troublesome when obesity is associated with sweating, urine incontinence and skin problems. Such ADL limitations may become so severe that basic self-care becomes difficult, especially for the morbidly obese. Obesity, especially morbid obesity, is also a risk factor for musculoskeletal pain, which may impair physical functioning and general well-being [68, 70-73]. Impaired physical functioning can result in low vitality [37, 43] and an impaired ability to fill social roles in daily life such as participating in paid work, parenting, housework and hobbies.

1.3.3 Social and emotional functioning and HRQL in morbid obesity

One of the greatest social challenges faced by morbidly obese persons is the stigma associated with the condition [32, 74]. The ancient Greeks used the term stigma to refer to the scarring or burn marks imprinted onto slaves, criminals or traitors to symbolize their societal status. Today, the term is used in a similar but more subtle way. The Canadian sociologist Erving Goffman's theoretical framework on stigma [75] and social interaction [76] explains the phenomenon of stigma as the categorization of an individual into a discrediting social

identity. According to Goffman, the (external) stigma of the individual will be internalized as the individual eventually accepts his or hers stigma, even though it is discrediting. In obesity, this internalization of (external) stigma may lead to an acceptance of having an undesirable body appearance and its implied character defects. This may in turn lead to the poor social interaction and impaired emotional quality of life that many morbidly obese individuals report.

The prejudice and stigma directed against obese individuals begins early in life. In 1967, J. Robert Staffieri reported anti-fat attitudes among 90 boys aged 6-10 years old [77]. The children were to apply 39 different adjectives to 3 silhouettes (thin, normal and overweight). The overweight silhouette was characterized as "cheats", "lies", "argues", "lazy", "sloppy", "mean", "dirty", "ugly", and "stupid" by the children. Later studies have produced similar results [78, 79]. Even studies of health personnel show anti-fat attitudes [80-82]. Such anti-fat attitudes among health personnel can make morbidly obese individuals reluctant to seek medical assistance for their condition and for the comorbidity associated with obesity. One Swedish population based study reported that obese individuals were twice as likely to report healthcare discrimination as healthy weight individuals [83], with the same reported in several other studies [84-86], suggesting that health care workers also stigmatize their obese patients.

A UK study of randomly selected subjects (n = 13,800, response rate 64%) applied the SF-36 [87] and found that overweight and obesity were associated with decreasing levels of both physical and emotional well-being. The authors also found that this deterioration in health status was more evident in the physical than mental dimension. In the mental and social domains overweight and obese subjects scored no less than underweight subjects. However, generic instruments like the SF-36 may not be tailored to measure mental, social and emotional HRQL in obesity. A study applying a disease specific instrument (OWLQOL) in

6107 obese subjects in the USA, Italy and France found that obese women had a consistently lower emotional HRQL than men (regardless of age or culture) and that the deterioration of emotional HRQL was significantly associated with increasing BMI [67]. Studies of another disease specific instrument (Impact of Weight on Quality of Life - IWQOL) have shown similar results [42, 43, 88]. These findings underscore the gender differentiated association between increasing BMI and decreased emotional HRQL. These studies also illustrate the importance of combining generic and disease specific instruments in clinical HRQL research.

1.3.4 Mental health and HRQL in morbid obesity

While many morbidly obese individuals have a good mental health, a number of studies have shown significant associations between obesity and impaired mental health. This impairment encompasses both a wide range of psychiatric diagnoses and minor disturbances. In a nationally representative sample of US residents (n = 9,125, 26% BMI $\geq$ 30 kg/m^2), obesity was associated with an approximately 25% increase in mood and anxiety disorders as well as an approximately 25% decrease in substance use disorders [34]. The prevalence of eating disorders is generally high in the obese population, especially Binge Eating Disorder (BED) and Bulimia Nervosa (BN). The WHO World Mental Health Surveys found that in people with BMI $\geq$ 40 kg/m^2, 7.6% reported BES and 5.6% BN over the last 12 months [89]. It has been hypothesized [36] that mood disorders, especially depression, are potentiated in the morbidly obese due to greater prejudice, discrimination and stigma. In one US study of a nationally-representative sample [33] the BMI-depression relationship varied in terms of gender. There were no significant associations between BMI and depression among men, while women with the highest BMI's (BMI $\geq$ 29 kg/m^2) were 38% more likely to score in the depressed range than women with lower BMI's. A second US population study [31] found that obese women were 37% more likely than normal weight women to have experienced

major depression in the past year. Obese women also reported more suicidal ideation and were more likely to have made a suicide attempt in the past year.

The association between mood disturbances and impaired HRQL Is shown in a cross-sectional study of 306 morbidly obese individuals [90]. 46% had a BMI of 40-49.9 kg/m^2, 34% a BMI of 50- 59.9 kg/m^2, and 19% BMI $\geq$ 60 kg/m^2. Impaired HRQL was defined as a score of 1 SD below national means. Of all participants, impaired HRQL, as measured with the SF-36, was found in 78% (physical functioning), 45% (physical role limitations), and 52% (bodily pain). Depression was assessed by Becks Depression Inventory [91]. The authors found that these three HRQL-scales were significantly associated with symptoms of depression (all $p < .001$). BMI was not related to depression and the interaction of BMI and HRQL impairment was not found to be significant. [90]. The authors concluded that impairments to the completion of everyday activities, the experience of significant pain and the difficulty of fulfilling occupational roles were stronger determinants of mood disturbance than the severity of obesity. Similar results are found in other studies [35, 44, 92-94].

In sum, such studies show that obese individuals, particularly females and those individuals with morbid obesity are at risk of developing psychological distress, especially eating disturbances and depression, even though such distress does not necessarily rise to the level of a formal psychiatric diagnosis. As described above, being obese is a source of stigmatization, while the social pressure to conform to norms of thinness may be internalized and lead to high levels of psychological distress. Eunkyung Park [95] suggests that gender may function as a moderator by exerting more sociocultural pressure on women to conform to an idealized physique, subsequently leading to mood and depressive disorders.

1.3.5 Work related factors and HRQL

Obese individuals have greater problems in job settings than normal weight individuals [32]. A 2011 Swedish study demonstrated that obesity stereotypes amongst 153 managers predicted labour market discrimination in hiring situations [96]. The authors found a strong and consistent relationship between managers' anti-obesity bias and the probability that they would invite a normal-weight, but not an obese, job applicant for an interview [96].

Another Swedish study of 5019 individuals found that severely obese women reported greater workplace discrimination than obese men and normal weight women. 29% of the moderately obese included in the study (n = 1,235, BMI 30-34.9 kg/m^2) reported workplace discrimination. Among the severely obese (n = 283, BMI ≥ 35 kg/m^2) this figure was 33%. Compared to normal weight women (BMI 18.4-24.9 kg/m^2), moderately obese women had an adjusted OR (95% CI) of 1.23 (.93-1.70) of reporting workplace discrimination, while severely obese women had an OR (95% CI) of 1.97 (1.48-3.10). The OR (95% CI) for moderately obese men (n = 628) was 1.65 (1.18-2.30) and amongst severely obese men (n = 119) the OR (95% CI) was 1.17 (.69-1.97). [83].

There are also significant associations between obesity and sick leave. A review of 36 studies exploring the association between obesity and sick leave showed differences between countries [97]. In US studies, obese workers had about 1–3 extra days of absence per person per year compared with their normal-weight counterparts. In European studies, the corresponding difference was about 10 days. The study also showed a J-shaped relationship between BMI and the risk for a disability pension [97], indicating that underweight and obese persons have an increased risk of being unemployed. Obesity would thus seem to have consequences for the ability of obese subjects to both access and retain paid work. These

consequences affect both the individuals in question and their families, adding to the general burden of life as well as other obesity related problems [97, 98].

There has been little focus on the association between employment and HRQL in morbidly obese. A Norwegian study of 51 morbidly obese subjects treated with duodenal switch [98] demonstrated a statistically significant association between employment and the physical and mental dimensions of the SF-36. The study was, however, limited by a lack of adjustments for obesity-related comorbidities and conditions which might have influenced HRQL. In addition, no obesity-specific measure of HRQL was addressed.

1.4 Treatment of morbid obesity

The cornerstone of obesity treatment is behaviour change. Morbid obesity treatment can take the form of either a pharmaceutical, surgical or lifestyle intervention. Various pharmaceutical products have been plagued with safety concerns or patient non-adherence due to the unpleasant side-effects, with several promising products not receiving approval from the regulatory agencies in the US and EU. However, pharmacological research is intensive and several new products are in the pipeline and awaiting testing and approval [99].

1.4.1 Bariatric surgery

In 1952 the Swedish surgeon Viktor Henrikson conducted the first reported bariatric procedure when he performed a small bowel partial resection, and was followed in 1954 by the US surgeon Arnold J. Kremen who conducted jejuno-ileal bypass [100]. Since these initial procedures bariatric surgery has gained popularity, with Roux-en-Y Gastric Bypass (RYGB) accounting for > 90% of bariatric procedures in Norway [101] and > 50% worldwide [102, 103]. A Cochrane database systematic review of bariatric surgery published in 2009 found only limited evidence of the efficacy of RYGB when compared to four other bariatric

procedures [103]. Nevertheless, RYGB is regarded as the "gold standard" of bariatric surgery [103]. RYGB is a combined restriction and malabsorption technique, where the surgeon first divides the stomach into a small, proximal pouch and a separate, large, distal remnant (figure 1). The upper pouch is joined to the proximal jejunum through a narrow Roux-en-Y gastrojejunal anastomosis. As a result of the procedure the storage capacity of the stomach reduces to approximately 5% of its normal volume, with ingested food bypassing approximately 95% of the stomach, the entire duodenum, and a small portion (15–20 cm) of the proximal jejunum [104] .

Figure 1. Gastric bypass

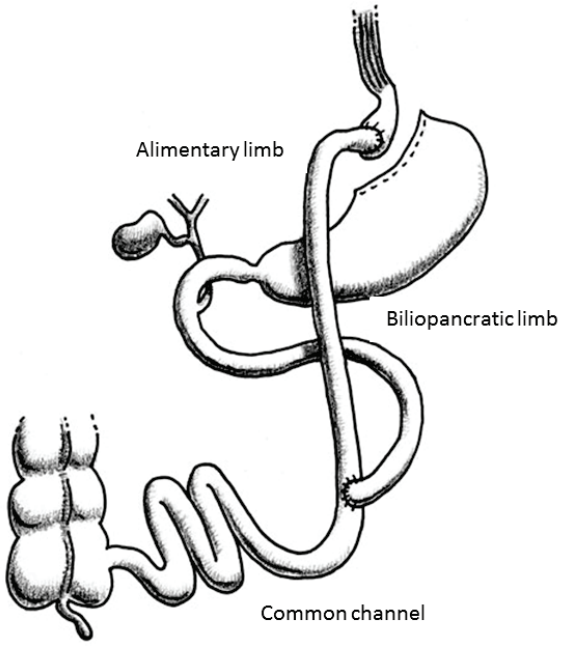


Illustration by Ole-Jacob Berge. Reproduced from Aasheim et al. [101] with permission.

The small gastric pouch forces the patient to eat carefully, with over-eating leading to stomach pain and/or vomiting/regurgitation. The 100-150 cm bypass of the proximal ileum

leads to reduced absorption of fat and other nutritional elements. In addition to these effects, the bypass of the stomach leads to a lower expression of appetite stimulating hormones such as ghrelin, as well as an increase in anorectic gut hormones such as glucagon-like peptide-1 and peptide YY [104-106]. Laparoscopic surgical techniques have fewer complications than open surgery, and today >90% of bariatric procedures are performed laparoscopically [107].

The Swedish Obese Subjects (SOS) study included 2010 obese subjects undergoing bariatric surgery [RYGB (13%), gastric banding (19%) and vertical banded gastroplasty (68%)], as well as 2037 contemporaneously matched obese control subjects receiving standard care. When comparing these bariatric procedures over a time span of 10-20 years, RYGB showed excellent short-term results and acceptable long-term results on weight loss, comorbidities [108, 109] and HRQL [110]. Even though RYGB seems to produce good results, postoperative complications occur in approximately 10% of cases [111]. The postoperative complications include deep venous thrombosis, anastomotic leaks, internal hernias, gastrointestinal bleeding, ulcers in the bypassed segments, torsion or volvulus of the roux limb, closed loop obstruction, stomal stenosis, wound complications, staple-line disruption, and gallstone formation following rapid weight loss [111]. Bypassing of the stomach and duodenum impairs the absorption of iron, calcium, thiamine and vitamin B12 [112, 113]. Other complications may also occur, such as vomiting, eructation, belching, diarrhoea, steathorrhoea, postprandial hypoglycaemia and dumping syndrome [114].

The dumping syndrome gives symptoms such as dizziness, nausea and headaches when glucose rich food is digested. These symptoms may occur very quickly. When eating fat rich food, bariatric patients are also at risk of steathorrhoea – troublesome acute fat diarrhoea. These side effects may also have an educative affect, with patients learning to avoid overconsumption as well as foods rich in glucose and fat.

1.4.2 Lifestyle intervention

Lifestyle intervention in overweight or obesity is a general term describing methods, therapies or treatments aiming to induce weight loss, health benefits and improvement of quality of life through an alteration of the individuals' behaviour in everyday life. Lifestyle intervention is a generic term and refers to different sorts of diets, training programs, coaching, counselling and psychological interventions. These may be individual or group based arrangements, be health professional led or not, and combine different methods. Lifestyle intervention programs can be carried out via the internet, in public, private or commercial facilities, in professional out-patient facilities or as a part of complex in-patient treatment programs.

A comprehensive lifestyle modification programme is recommended as a first step towards reaching weight loss goals [1]. Such comprehensive lifestyle modification programs usually consist of three elements; dietary intervention, physical activity and behavioural intervention [115]. Such comprehensive programs in obesity management are often termed intensive lifestyle interventions (ILI).

Dietary intervention

Reducing energy intake is an important aspect of weight reduction. This can be achieved by reducing the intake of certain macronutrients (protein, carbohydrate and/or fat), and gives rise to a variety of diets. Fat is the most energy dense of macronutrients, and low fat diets are often combined with a proportional increase of whole grain, fruit and vegetables to help obese and overweight individuals lose weight [116].

Diets aimed at changing the amount (and type) of carbohydrates are popular. The low glycaemic diets are based on how quickly food containing carbohydrates raises blood-glucose

levels. Different foods have varying effects on blood sugar levels, with low glycaemic diets advocating food with slow absorption carbohydrates, thereby balancing blood sugar levels and providing a higher degree of satiety. Another type of low carbohydrate diets are the ketogenic diets (high-fat, adequate to high-protein, very-low-carbohydrate). Carbohydrates contained in food are converted into glucose and then fuel body cells. If very little carbohydrate is digested, the liver converts fat into fatty acids and ketone bodies. The ketone bodies pass into body cells and replace glucose as an energy source. In a randomised study, 79 obese patients with type 2 diabetes were given either a low-fat diet or a low glycaemic diet for 40 weeks. There were no significantly different weight losses at 20 or 40 weeks, but patients with a low glycaemic diet had significantly greater improvements in glycosylated haemoglobin (HbA1c), indicating an improvement in their diabetic condition [117]. In a large scale trial 811 participants [mean (SD) age 51 (9) years, BMI 33 (4) kg/m^2, 64% females] were randomised to one of four diets with different macronutrient composition (fat, protein, carbohydrates: 20, 15, and 65%; 20, 25, and 55%; 40, 15, and 45%; and 40, 25, and 35%). All the diets were calibrated such as to have a daily 750 kcal deficit. After 2 years the authors found no significant difference in weight loss between groups, and concluded that reduced-calorie diets result in clinically meaningful weight loss regardless of which macronutrients they emphasise [118].

Low calorie diets and very low calorie diets are commercially popular and produce rapid weight loss. Critics of low calorie diets point to poor adherence in the long run and secondary weight regain. However, several studies indicate that greater initial weight loss improves long-term weight loss [119-124]. In a recent American study of 1685 multi-ethnic obese participants, weight loss at 6 months was found to be a consistent predictor of weight loss after 36 months across gender and ethnic groups [123]. The same was reported in a Swedish

study of 247 participants undergoing a two-step weight loss program lasting for 8–10 months. The strongest factor for predicting weight loss in the Step II treatment was Step I weight loss. Each 1 kg weight loss in Step I predicted 13% of the variation in Step II weight loss [119]. The randomised multi-centre Look Ahead-study found that the larger a participant's weight loss was after the first year, the larger their loss at year 4. The odds of achieving a loss ≥ 10% of baseline weight at year 4 were 9.8 (95% CI: 6.99–13.74) times greater for participants who lost ≥ 10% at year 1 compared to participants who lost <5% at year 1, and 2.0 (95% CI: 1.41–2.96) times greater for participants who had lost 5.0–9.9% at year 1 compared with those who lost < 5% at year 1 [124].

A Finnish study examined obese hospital outpatients undergoing a 10 week low calorie diet followed by 4 month group sessions, assessing the development of HRQL changes after years 1 and 2. The 100 patients [mean (SD) age 48 (11) years, BMI 43 (6) kg/m^2, 66% women] finishing treatment lost 12.5% of baseline weight and improved all HRQL scales markedly. After 2 years mean weight regain was two thirds of the lost weight and HRQL improvements were maintained only in the psychosocial and physical functioning domains. The subgroup with ≥ 10% maintained weight loss maintained a cluster of positive HRQL improvements relative to baseline [125].

Physical activity

Physical activity (PA) is considered an integral part of weight management. In 2001 the American College of Sports Medicine (ACSM) recommended [126] a minimum of 150 minutes per week of moderate-intensity PA for overweight and obese adults to lose weight. Obese adults should progressively increase this exercise goal. In 2009 the ACSM pointed out that recent evidence supported this recommendation but also indicated more PA to be

necessary [127]. The ACSM found that moderate-intensity PA (between 150 and 250 minutes per week) provided only modest weight loss, and that a greater amount of PA (> 250 minutes per week) was associated with a clinically significant weight loss. In a two year randomised trial 201 overweight and obese women [mean (SD) BMI 33 (4) kg/m^2, age 38 (6) years] were assigned to 1 of 4 groups based on physical activity energy expenditure (1000 vs. 2000 kilocalories per week) and intensity (moderate vs. vigorous) [128]. Energy expenditure was converted to minutes per week based on the average body weight of participants and weekly goals were expressed in minutes per week. Participants were encouraged to spread the exercise over 5 days per week and to exercise for a minimum of 10 minutes each time. Intensity was prescribed as percentage of age-predicted maximal heart rate (moderate, 50-65%; vigorous, 70-85%) and rating of perceived exertion (moderate, 10-12; vigorous, 13-15). After 2 years there were no significant differences between groups and all groups regained weight between years 1 and 2 [128].

The ACSM positional statement suggests that PA on its own is of limited benefit in terms of inducing weight loss [115]. However, weight loss is not the only end point of PA. There is no doubt that regular PA contributes to the prevention of cardiovascular disease, diabetes, cancer, hypertension, obesity, depression and osteoporosis, and is moreover associated with a reduced risk of premature death [129] as well as improvement of HRQL [130, 131].

Behaviour intervention

Traditionally, behaviour intervention in obesity management has been based on the assumption that behaviours regulating body weight are learned, and thus can be relearned or modified [132]. Today, most researchers believe that body weight is also affected by factors other than behaviour. These include genetic, metabolic and endocrine influences [133].

During the last two decades, cognitive elements have been added to the behaviorual component of obesity management. The underlying assumption is that thoughts (cognitions) directly affect feelings and behaviours [133] and that negative feelings are associated with negative outcomes.

Behaviour intervention is goal directed, process oriented and advocates small rather than large changes [133, 134] and consists of some common components; self-monitoring (food and activity records), eating stimulus control, nutrition education, slowing eating, physical activity, problem solving, and cognitive restructuring [132, 133].

A review of 9 meta-analyses and systematic reviews comprising 198 trials with > 23,000 participants on lifestyle interventions for obesity (between 1999 and 2009) found little evidence to indicate that any one component (ie. diet, PA, behavioural/cognitive) was more effective than any other [135]. However, there seemed to be an additive effect when combining the components in the treatment of obesity.

Intensive behavioural intervention in specialized weight loss centres can be a safe and effective treatment option for severely obese individuals. In one study [136], 1100 morbidly obese patients [mean (SD) BMI 49 (8) kg/m^2, age 44 (11) years, 63% women] completed a 12-week "Core-intervention" class with follow-up until participants reached their weight goal and entered a maintenance phase. The maintenance phase included weekly meetings and telephone calls, record keeping, restricted energy intake and physical activity. The mean (SE) weight loss was 25 (.01) % of initial weight after mean (SE) 39 (1) weeks. Weight loss after 72 weeks was on average 23 kg (59% maintained weight loss). 24% (n=268) had a mean weight loss of 40% in an average of 57 weeks [136].

Not only may the content of an ILI have an impact on outcomes, but also its structure. Martins et al. [137] studied the association between the structure of a 2 year residential intermittent ILI program (totaling five stays) for morbidly obese, weight loss and cardiorespiratory fitness. This retrospective follow up study [n = 179, mean (SD) BMI 44 (6) kg/m^2] compared 81 participants with a first stay of 8 weeks (total length of stays = 18 weeks, group A) with 98 participants with a first stay of 2 weeks (total length of stays = 12 weeks, group B). After 2 years, the completers in group A (n = 52) had a mean (SD) weight loss of 13 (10) % versus group B (n = 65) of 6 (9) % ($p < .001$). The same pattern was observed when measuring changes in cardiovascular fitness. There was a larger improvement in peak oxygen uptake at both 1 and 2 years in group A compared with group B [7.8 vs. 3.6 ml/kg/min ($p < 0.01$) and 5.6 vs. 2.5 ml/kg/min, ($p < 0.01$), respectively] [137]. Another Norwegian study [138] found that morbidly obese subjects following a 10-14 week ILI at a rehabilitation centre lost a mean (SD) of 15 (9)% of baseline weight at 12 months. Neither study examined changes of HRQL.

Other studies of ILI have shown promising HRQL results. Gjevestad et al. [139] showed that a 1 year outpatient ILI at a public tertiary care centre was associated with significant mean (95% CI) weight loss of 10 (9-12)% and improved physical HRQL of mean (95% CI) 7 (4-9) points (ES = .54), mental HRQL of 4 (1-7) points (ES = .18) and emotional HRQL of 18 (13-23) (ES = .77). A *moderate* outpatient lifestyle intervention program at a public secondary care centre was associated with only limited beneficial effects on weight loss and HRQL.

Few studies have addressed the comparative effects of bariatric surgery and lifestyle intervention on HRQL. The SOS-study compared patients undergoing various bariatric procedures with patients undergoing conventional weight-loss treatment [110]. Notably, treatment for the conventionally treated patients was not standardised and treatment regimens varied according to local practice. After 10 years, the study showed that patients who chose surgery lost about 15 times more weight than non-surgically treated patients, mean (SD) loss

of 19.7 (15.8) kg vs. 1.3 (13.8) kg. HRQL improved to a significantly greater extent in the surgery group (compared to the non-surgically treated group) in the domains of current health perception, social interaction, psychosocial functioning and depression. No significant between group differences were found for overall mood and anxiety. This effect was mainly explained by weight loss. Notably, the study did not predefine the lifestyle intervention for the non-surgical groups, which makes comparison between bariatric surgery and lifestyle programs difficult. In general, there is limited comparable evidence regarding HRQL following RYGB and specific predefined comprehensive and multidisciplinary lifestyle intervention.

In addition, most studies of HRQL in morbid obesity have focused on the physical and mental aspects, applying generic instruments of HRQL measurement. The development of obesity-specific HRQL instruments enables additional analyses of the emotional and symptomatic dimensions. Furthermore, only a few studies of morbidly obese HRQL have calculated the clinical relevance of HRQL-change after treatment.

2. Aims of the thesis

The aim of this thesis was to explore and investigate three research questions;

1. Is the HRQL of treatment-seeking morbidly obese subjects associated with employment status?

2. Is bariatric surgery more effective than intensive lifestyle intervention in terms of improving HRQL?

3. Does the structural validity of the SF-36 hold in a population of morbidly obese treatment seeking subjects?

These research questions led to the following hypotheses:

Paper I:

Employment is associated with higher HRQL in treatment seeking morbidly obese persons.

Paper II:

Bariatric surgery provides greater improvements in HRQL than intensive lifestyle intervention.

Paper III:

The structural validity of the SF-36 is high in a population of morbidly obese treatment seeking patients.

3. Material and methods

3.1 Participants and study design

Two of the studies (paper I and paper II) underlying this thesis are based on data from the non-randomised pragmatic clinical MOBIL-study (Morbid Obesity treatment, Bariatric surgery versus Intense Lifestyle intervention, Clinical Trials.gov number NCT00273104), which was designed to compare the efficacy of bariatric surgery and intensive lifestyle intervention on various comorbidities, eating behaviour and HRQL. All patients were morbidly obese and referred from secondary health care clinics to the Morbid Obesity Centre at Vestfold Hospital Trust, located in Tønsberg, Norway.

One cross-sectional validation study (paper III) is based on data from Evjeklinikken AS, a rehabilitation centre specialising in intensive lifestyle intervention (ILI) in morbid obesity. Evjeklinikken AS is located in Evje, Norway. Patients were referred to the rehabilitation centre from both the Morbid Obesity Centre and from secondary health care clinics under the South Eastern Regional Health Authority in Norway.

Table 1. Study design, population and sample size of the three studies.

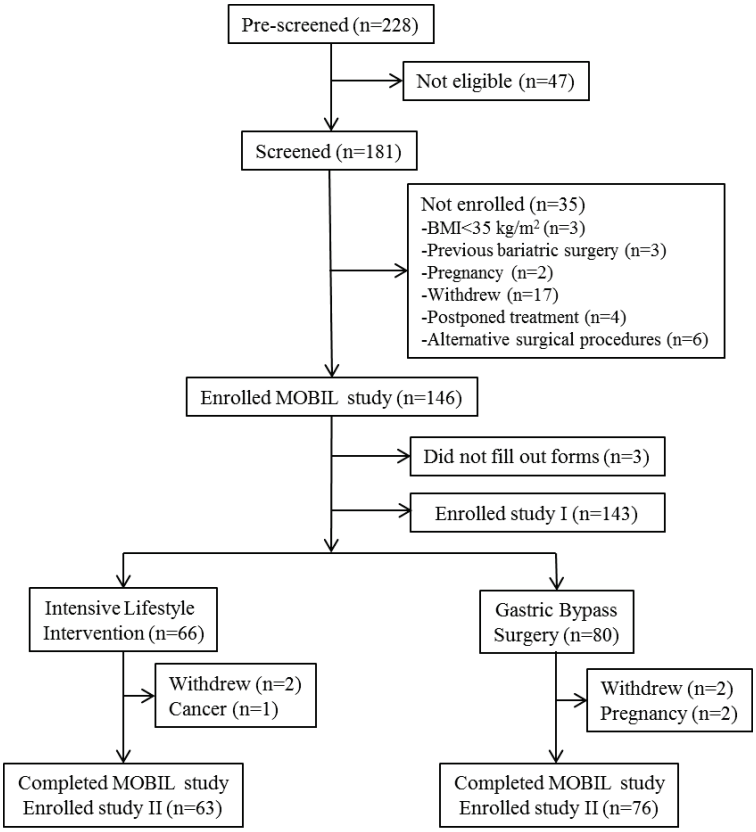
Paper	Study design	Population	Sample size
I	Pragmatic non-randomised clinical trial/cross-sectional analysis (baseline data)	Morbidly obese treatment seeking patients	143
II	Pragmatic non-randomised clinical trial	Morbidly obese treatment seeking patients	139
III	Cross-sectional validation	Morbidly obese treatment seeking patients	475

All studies were approved by the Regional Committees for Medical and Health Research Ethics and performed in accordance with the Helsinki protocol.

3.1.1 The MOBIL-study (paper I and II)

Paper I and II included patients from the MOBIL-study. The flow of patients is shown in figure 2.

Figure 2. Flow of patients (paper I and II)



Between December 2005 and May 2006 a total of 228 first time patients attending the Morbid Obesity Centre were pre-screened for participation in the study. A total of 181 patients satisfied the inclusion criteria for bariatric surgery and desired either RYGB surgery or ILI.

Finally, 146 patients were accepted for either RYGB (n = 80) or ILI (n = 66). Three patients did not fill out HRQL-questionnaires [either not at all (n = 2) or with > 90% missing items (n = 1)], leaving data from 143 patients to be included in paper I. One year follow up was completed by June 2009. A total of 139 patients (95%) completed the study and data from these completers is explored in paper II.

All surgical procedures were performed at the Morbid Obesity Centre at Vestfold Hospital Trust, and the majority (59/63) of patients in the lifestyle group were referred to a rehabilitation centre specialising in the care of morbidly obese patients (Evjeklinikken AS).

3.1.2 Cross-sectional validation study (paper III)

Paper III was based on data collected at Evjeklinikken AS. In order to reduce potential selection bias, all patients with morbid obesity (n = 537) admitted to the rehabilitation centre between May 2005 and September 2009 were sent the SF-36 prior to their first admission. All subjects (n = 537) were non-immigrants of Caucasian ethnicity. Of these, 62 (11%) patients had more than 60% missing item values, leaving 475 (89%) patients eligible for further statistical analysis.

3.2 Interventions

Two major interventions were applied; Roux-Y-Gastric Bypass (RYGB) and intensive lifestyle intervention (ILI).

3.2.1 Surgical intervention

Patients in the RYGB group completed a low-calorie diet (3.3–3.8 MJ/day) 3–6 weeks before surgery [140]. Laparoscopic RYGB was performed in 74 of the 76 surgically treated patients.

The gastric pouch was about 25 ml, while the median (range) of alimentary limb was 120 (80–250) cm; biliopancreatic limb 100 (50–170) cm; and common channel, variable length. The bariatric surgeons tended to choose longer limbs in the heaviest patients. After surgery, a standardised regimen of dietary supplements [112] and a proton pump inhibitor were prescribed to all patients. Patients with a high risk of venous embolism were prescribed low-molecular weight heparin. During follow-up, patients allocated to surgery were examined by a bariatric surgeon 6 weeks post-surgery, while groups of patients were seen by a registered dietician quarterly. To optimise the result of the procedure patients were encouraged, both before and after the surgery, to normalise their eating behaviour and to increase their physical activity level [140].

3.2.2 Lifestyle intervention

The lifestyle intervention is best described as a partly residential multidisciplinary intensive lifestyle-intervention program. The treatment goal for individual participants was to lose approximately 10% of their baseline body weight. Each patient was encouraged to increase their physical activity and to normalise eating habits. The programme intended to increase the patients' self-efficacy in dealing with their weight problem, as well to improve their self-esteem.

The 1-year ILI comprised of four stays at a rehabilitation centre – three 5-day stays in weeks 1, 26, and 51, and a four-week stay from weeks 13–17 (figure 3).

Figure 3. Structure of stays at the rehabilitation centre

The daily schedule was divided between organised daily physical activity of varying intensity (3–4 hours); walks, swimming, bicycling, gymnastics, yoga, and football. The daily schedule also included various individual and group based psychosocially oriented interventions combined with a motivational approach (3–4 hours), and moreover included consultations with a medical doctor, registered dieticians, physiotherapists and mental health trained nurses.

No special diet or weight-loss drugs were prescribed, but patients were encouraged to follow the guidelines of the Norwegian National Council of Nutrition [141], which recommends that the daily intake of protein, fat, carbohydrate and alcohol should account respectively for 10–20, <30, 50–60, and <5% of energy consumed. In addition, the patients were asked to reduce their daily total energy intake, but not using calorie counting. Nutritional advices were conveyed to the patients through individual consultations and group sessions with registered dieticians. Outside their stays at the rehabilitation centre, patients were contacted by phone once every second week and were also encouraged to consult their GP for weight measurement and follow-up every four weeks. They were also encouraged to self-monitor eating habits and physical activities on a daily basis in a prefabricated paper based diary. In the diary, patients were to mark what kind of meals they had eaten, approximately how many steps they had taken, their main daily activities and their "food temptations". They were also encouraged to write a few words describing their emotions that day. The patients were also instructed to bring the diary to their GP.

3.3 Variables

3.3.1 Outcome variables

In sum, three HRQL instruments (SF-36, OWLQOL and WRSM) constitute five different measurements of HRQL; physical HRQL (SF-36 physical component score), mental HRQL (SF-36 mental component score), emotional HRQL (OWLQOL total score), number of

obesity symptoms (WRSM symptom count), and distress of obesity symptoms (WRSM symptom distress core). The primary outcome variables in papers I-III were the scores on HRQL-instruments measuring physical HRQL, mental HRQL, emotional HRQL (paper I), physical HRQL, mental HRQL, emotional HRQL, number of obesity symptoms, and symptom distress (paper II). In paper III, only SF-36 was under study.

3.3.2 Explanatory variables

All participants underwent a medical examination by a physician during their first consultation. Demographic data, socioeconomic history and medical history were recorded. Weight and height were measured with patients wearing light clothing and no shoes. BMI was calculated as weight in kilograms divided by the square of the height in metres. Blood pressure was measured three times after at least 5 minutes rest, at the right or left brachial artery, with the patient in a sitting position. The average of the second and third measurements was registered. Hypertension was confirmed if either systolic blood pressure was greater than 140 mm Hg, if diastolic blood pressure was greater than 90 mm Hg, or if the patient received antihypertensive drugs. All patients underwent one overnight sleep registration with a portable monitor, the Embletta™ system; which has both high sensitivity and specificity when compared to the "gold standard" overnight polysomnography used to identify obstructive sleep apnoea (OSA) [105]. OSA was diagnosed for patients with moderate to severe sleep apnoea [apnoea–hypopnea index (AHI) ≥ 15 events per hour] as these patients are more likely to have symptoms than those with mild OSA. Type 2 diabetes was diagnosed in patients treated either with glucose-lowering drugs or with a fasting glucose ≥ 7.0 mmol/l and/or a 2-hour glucose ≥ 11.1 mmol/l after the ingestion of a 75-g anhydrous glucose solution [106]. In addition, all patients completed a questionnaire about their diet and physical activity [107]. Patients were categorised as having a sedentary lifestyle if they had no (less than 10 min a

week) aerobic moderate or vigorous activity based on their answer to the following question: "Do you perform any physical activity and exercise making you a little short of breath (more than 10 min a week bicycling, swimming, walking, skiing, dancing, or golfing)?"

3.3.3 Assessment of change scores (paper II)

The two interventions were expected to affect HRQL scores. These HRQL changes might be assessed statistically and statistical significance may be calculated as a p-value. However, statistical significance does not always imply clinical relevance and for many clinicians, the unfamiliarity of the different HRQL scales may cause uncertainty as to how to interpret the results. Calculating effect size (ES) by Cohen's *d* is one way to assess the clinical relevance of change scores on a HRQL-instrument pre and post treatment [142-144]. Cohen´s *d* is understood as the standardised difference between two means [143] and is defined by Jacob Cohen [145] as the average change from pre-test to post-test divided by the standard deviation at baseline. Norman et al. compared the responsiveness of Cohen's *d* against 9 other indices (standardized effect size, normalized ratio, responsiveness statistic, Guyatt responsiveness, standardized response mean, reliable change index, unpaired T-test, and paired T-test) on observed change scores on measure of health status (n = 50). The authors concluded that Cohen's *d* is the most appropriate measure, as it provides unique information and captures an important relation between treatment effect and variability in response. The authors recommend that future analysis of responsiveness should be restricted to Cohen's *d* in order to ensure interpretability and comparability with treatment effects in other domains.

This also implies that Cohen's *d* is applicable on different scales in the same intervention. The standardized changes can be compared using the same unit of measure (SD), despite the scales having different ranges of values [143-145]. In addition, Cohen's *d* provides a general set of thresholds or benchmarks as to the impact of an intervention, with a Cohens *d* from .20–

.49 to be considered small, .50–.79 as moderate, and greater than .80 as large [143, 144]. Cohen's *d* is from hereafter referred to as effect size (ES).

3.4 Statistical methods

Data are presented as mean (SD) or n (%) unless otherwise stated. Skewed data were transformed to approximate normality using natural logarithms. To assess the reliability of the HRQL scales we calculated Cronbach's alpha coefficients.

Within-group analyses were performed using paired samples t-test. Between-group comparisons at baseline were analysed using independent samples t-test for continuous variables and χ^2 or Fisher's exact test for categorical variables. Two-tailed P values are reported; with $p < .05$ was considered to be statistically significant.

In paper I we also performed three multiple linear regression analyses, with physical, mental and emotional HRQL as dependent variables. Ten predefined explanatory variables were included in each model. In examining the variation of inflation factors in the models we found no consequential multicollinearity between the independent variables. The probability–probability plot between expected and observed cumulative distribution was considered acceptable. Semi-partial (part) correlation coefficients were squared in order to calculate the percentage of total variance in the dependent variable explained by a given independent variable.

In paper II, after applying Little's test of randomness for missing data, missing values (SF-36: 23.5%, OWLQOL: 24.5%, WRSM: 23.7%) were imputed using multiple imputation. The imputation model consisted of the following predictor and imputation variables: five HRQL-scores (physical, mental, and emotional dimensions and number of obesity symptoms and symptom distress), physical activity at baseline and 1 year, and age of onset of obesity.

Treatment, gender, age, baseline BMI, marital status, employment and education were included as predictor variables only. Through a fully conditional specification model, applying linear regression as the prediction method for scale variables and two-way interactions for categorical variables, we generated 20 complete datasets for each of the HRQL-scores with 10 iterations per dataset. The statistical analyses were performed within each complete dataset, and thereafter the multiple analyses results were combined to achieve single estimates. The combined estimates are presented.

Within groups ES was calculated as the mean HRQL change score between 1 year and baseline divided by the standard deviation of the baseline HRQL. Between groups ES was calculated as the difference in mean HRQL change score between groups at 1 year divided by the standard deviation of baseline HRQL of the sample [143, 144].

In order to reduce problems of regression towards the mean [146, 147], we applied five one-way analyses of covariance (ANCOVA) to compare the effect of RYGB and ILI on the five dimensions of HRQL between groups. Age at baseline, age at the onset of obesity, BMI at baseline, physical activity at baseline, and baseline HRQL-scores were used as covariates in each of the five analyses [148]. Assessments of normality, linearity, homogeneity of variance and regression slopes were conducted to ensure assumptions for the ANCOVA. The unadjusted changes from baseline in the RYGB group and ILI group together with the adjusted between group differences (95% CI) are reported. To account for the percent explained variance in the dependents, calculations of partial eta squared (ηp^2) were performed. To test the effect of weight reduction (instead of treatment choice) on HRQL multiple linear regression analyses were conducted with each of the 12 months HRQL changes (physical, mental, and emotional dimensions, number of obesity symptoms, and symptom distress) as dependents, and with the following as independents: gender, age at

baseline, age at the onset of obesity, BMI at baseline, physical activity at baseline, and weight change as percent of baseline weight.

In paper III we examined the component structure of the SF-36 and applied a PCA with an oblique (promax) rotation [149, 150]. The Kaiser-Meyer-Olkin measure and Bartlett's test of sphericity were computed to determine whether the data in this sample were suitable for PCA. How many factors to retain is a critical component of exploratory factor analysis. Following Kaiser's criterion, eigenvalues of 1.0 were chosen to ensure that the extracted components accounted for a reasonably large proportion of the total variance [150]. Methodological research has shown that the Kaiser's criterion may include too many components [149, 151]. A parallel analysis [149] was conducted to affirm the extraction. Parallel analysis involves comparing the eigenvalues from the actual sample with those obtained from a randomly assigned dataset. A correlation matrix is calculated from the randomly generated dataset, and the eigenvalues of the correlation matrix are computed. Components corresponding to the initial eigenvalues that are greater than the parallel average random eigenvalues should be retained. An item was considered to be loaded on a component if coefficients were 0.32 or larger [150]. To assess the model fit, we applied confirmatory factor analyses (CFA) as structural equation modelling. Two tests of goodness of fit were used to evaluate the models, the Comparative Fit Index (CFI) and the Root Mean Squared Error of Approximation (RMSEA). A CFI > 0.90 indicates that the model has a good fit to the data. RMSEA < 0.08 indicates a good fit to the data, while values > 0.10 suggest that the model fit is unsatisfactory [150].

The statistical analyses in the three papers were conducted using SPSS Statistics v. 17.0-18.0 (SPSS Inc., Chicago, IL, USA/ IBM Corp., Armonk, NY, USA), PRELIS v. 8.8 (SSI Inc., Lincolnwood, IL, USA) for principal component analyses, Windows MonteCarlo PCA for

parallel analysis, and AMOS v. 18.0 (IBM Corp., Armonk, NY, USA) for confirmatory factor analysis.

4. Results

4.1 Paper I

Our study demonstrated that in morbidly obese patients allocated to either surgical treatment or lifestyle intervention, controlling for age, gender, current BMI, obesity history, marital status, and comorbidities, employment was independently associated with both the physical and mental aspects of HRQL as measured with the SF-36. Conversely, employment was not associated with the emotional aspects of HRQL as measured with the OWLQOL (table 3).

Table 3. Predictors of HRQL in 143 morbidly obese patients (paper I)

QOL dimension	Physical, R^2 =0.36, Coeff.	Mental, R^2 =0.17, Coeff	Emotional, R^2 =0.26, Coeff.
Gender	0.13	0.15	0.51***
Age	-0.22*	0.07	0.07
BMI	-0.09	0.13	-0.15
Marital status	-0.09	-0.02	0.05
Education	-0.07	-0.06	0.01
Employment	0.43***	0.33**	0.07
Hypertension	0.03	0.01	0.16
OSA	-0.09	-0.03	0.06
Type 2 diabetes	-0.14	-0.11	-0.04
Seeking surgery	0.26**	0.12	0.13

Standardized (beta) regression coefficient values are given. Linear regression; * $p < 0.05$, **$p < 0.01$, ***$p < 0.001$

Squared part correlations showed that employment explained 16% of the variation in the physical HRQL and 9% of the variation in the mental HRQL. Gender explained 22% of the variation in the emotional HRQL.

4.2 Paper II

We found that the effectiveness of RYGB was greater compared to ILI in improving HRQL after 1 year. Within the RYGB group all HRQL dimensions showed large improvements. Within the ILI group, all HRQL changes were small to moderate.

The inter-item analyses showed Cronbach's alpha coefficients > .80, indicating that intercorrelations among the items was high and thus that there is a high reliability for all of the HRQL-scales (physical, mental, and emotional dimensions, number of symptoms, and symptom distress).

Compared to the ILI group, the patients in the RYGB group had a higher BMI (ES = .49), were younger (ES = .36), had earlier onset of obesity (ES = .47), and had lower physical (ES = .50) and emotional HRQL (ES = .42). All patients in the RYGB group lost more than 15% of their baseline weight. In the ILI group 62% lost ≥ 5% and 38% lost ≥ 10% of their baseline weight.

Adjusted between group analyses, controlling for age at baseline, age at the onset of obesity, BMI at baseline, physical activity at baseline, and baseline HRQL-scores, showed that the RYGB group had statistically significant higher adjusted mean improvement in all HRQL-measurements, especially emotional HRQL (table 4). Based on calculations of ηp^2, type of treatment predicted 19.7% of the variance (ES = .83) in the physical dimension change score, 9.8% (ES = .50) in the mental dimension change score, 22.6% (ES = 1.06) in the emotional dimension change score, 7.7% (ES = .56) in the number of symptoms, and 8.1% (ES = .37) in the symptom distress change score.

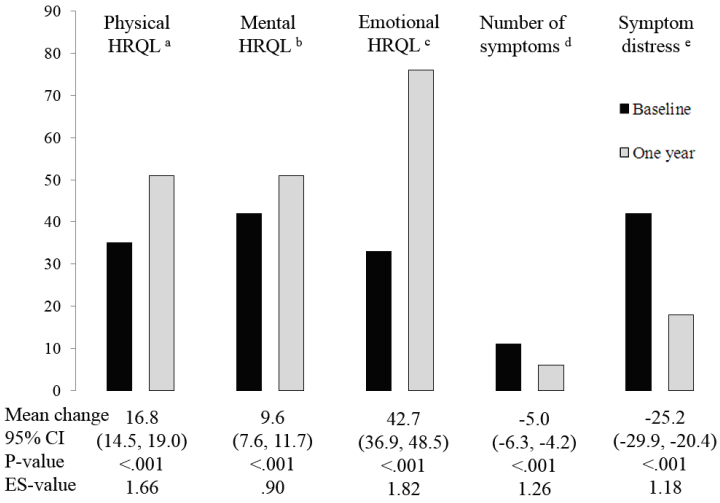
Table 4. One way between-groups analysis of variance on five dimensions of HRQL in morbidly obese patients undergoing either RYGB or ILI. (paper II)

	Changes from baseline				
	RYGB (n=76)	ILI (n=63)	Adjusted between group difference, mean (95% CI)	P	ES
Physical dimension[a]	16.8 (9.7)	4.9 (9.4)	8.6 (4.6,12.6)	<.001	.83
Mental dimension[a]	9.6 (9.1)	3.5 (8.9)	5.4 (1.5,9.3)	.007	.50
Emotional dimension[b]	42.7 (25.5)	15.7 (21.7)	25.2 (15.0,35.4)	<.001	1.06
Number of obesity symptoms[c]	-5.3 (4.6)	-2.9 (4.7)	-2.3 (-4.5,-.6)	.012	.56
Symptom distress[d]	-25.2 (20.7)	-14.3 (16.5)	-8.7 (-15.4,-1.8)	.013	.37

Adjustments were made for age at the onset of obesity and baseline values of age, BMI, physical activity level, and HRQL. (a) SF-36 (scale 0-100). (b) OWLQOL (scale 0-102). (c) WRSM (scale 0-20). (d) WRSM (scale 0-120). Statistical significance (P) and effect size (ES) are reported.

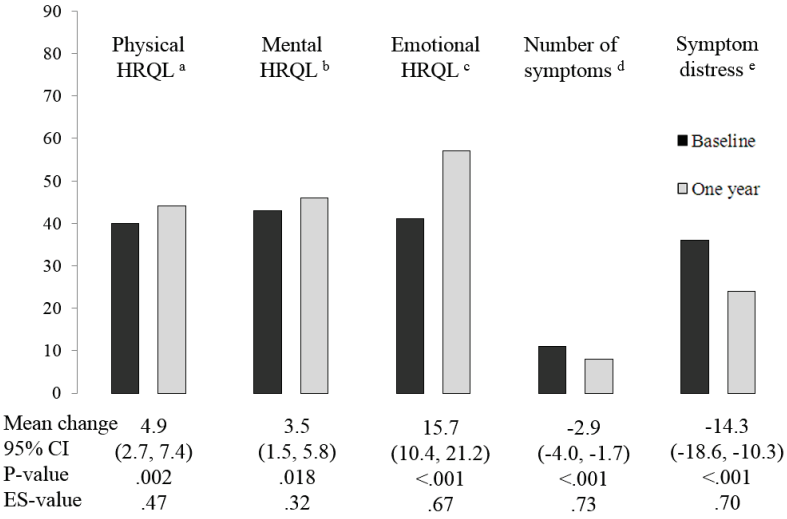
Unadjusted within-group analyses showed that both groups reported improvements in all five HRQL-measurements (figure 4 and 5).

Figure 4. Mean scores on five HRQL-scales at baseline and 1 year in morbidly obese patients who underwent RYGB (n=76) (paper II).



(a, b) SF-36 (scale 0-100). (c) OWLQOL (scale 0-102). (d) WRSM (scale 0-20). (e) WRSM (scale 0-120).

Figure 5. Mean scores on five HRQL-scales at baseline and 1 year in morbidly obese patients who underwent a partly residential intensive lifestyle intervention program (n=63) (paper II).



(a, b) SF-36 (scale 0-100). (c) OWLQOL (scale 0-102). (d) WRSM (scale 0-20). (e) WRSM (scale 0-120).

Compared to the ILI group, the RYGB group showed greater improvement in problems such as reduced physical stamina, joint pain, snoring, sleep problems, skin irritation, water retention, and foot problems. Only the improvements of physical stamina and joint pain showed large effect sizes between groups. On the other hand, the RYGB group reported higher sensitivity to coldness, and this difference was considered large.

The multiple linear regression analyses of weight reduction (instead of treatment choice) on HRQL showed a standardized (beta) coefficient of -.430 ($p < .001$) on the physical dimension, -.288 ($p = .004$) on the mental dimension, -.432 ($p < .001$) on the emotional dimension, .287 ($p = .008$) on number of symptoms, and .274 ($p = .009$) on reduction of symptom pressure.

4.3 Paper III

The summary scales of the SF-36 had satisfactory construct validity in treatment seeking morbid obese patients. The construct validity of the subscale scores was, however, weak. Table 5 shows the items of the SF-36 loaded on 6 components when tested in a sample of 475 Norwegian morbidly obese patients seeking intensive lifestyle intervention.

When forcing the PCA into a 2-component extraction, the items loaded into a physically and a mentally oriented domain (table 6).

The analyses of model fit show an acceptable fit for the 6-component model (RMSEA = .08, CFI = .81) (table 5) and an unacceptable fit for the original 8-component model (RMSEA = .13, CFI = .47) (data not shown). The 2-component model has acceptable fit, both as a second order model (RMSEA = .08, CFI = .84) (data not shown) and as a single item model (RMSEA = .07, CFI = .88) (table 6).

Table 5. Rotated structure in a 6-component PCA, oblique (promax) rotation; presenting item loads of the SF-36 on components 1–6 (items with loadings ≥ 0.32 in bold) for morbidly obese patients (n = 475) (paper III)

			Components					
Items	Item text	Sub-scale	1	2	3	4	5	6
sf3a	"Health limits vigorous activities"	PF	**.64**	-.10	.00	-.07	-.12	-.04
sf3b	"Health limits moderate activities"		**.58**	.26	-.10	.05	.07	-.02
sf3c	"Health limits lifting and carrying groceries"		.06	**.49**	-.02	.22	.06	-.01
sf3d	"Health limits climbing several flights of stairs"		**.76**	.18	-.02	-.15	-.06	-.03
sf3e	"Health limits climbing one flight of stairs"		**.40**	**.55**	-.05	-.13	.04	-.01
sf3f	"Health limits bending, kneeling or stooping"		**.76**	.08	-.05	-.01	-.09	-.09
sf3g	"Health limits walking more than a mile"		**.62**	**.38**	.05	-.11	-.12	-.02
sf3h	"Health limits walking several hundred yards"		.20	**.80**	.06	-.05	-.03	.05
sf3i	"Health limits walking one hundred yards "		-.10	**.90**	.07	.02	.00	.05
sf3j	"Health limits bathing or dressing yourself "		.18	**.39**	-.14	.05	.10	.05
sf4a	"Due to physical health cut down time on work"	RP	.25	.14	.13	.26	.04	.06
sf4b	"Due to physical health accomplished less"		**.45**	.00	.21	.13	-.13	.18
sf4c	"Due to physical health limited in work"		**.53**	.00	-.03	.27	.01	-.08
sf4d	"Due to phys. health difficulty perform. work"		**.61**	.02	.03	.15	.01	-.08
sf7	"Bodily pain"	BP	.07	.01	-.01	**.79**	-.09	.08
sf8	"Pain interfered with normal work"		.13	-.01	.01	**.85**	-.01	.00
sf1	"Self reported health"	GH	**.47**	.13	-.04	.09	.17	-.04
sf11a	"Seem to get ill more easily than other people"		.18	-.09	.04	.14	.26	-.08
sf11b	"As healthy as anyone I know "		.28	-.04	-.02	.16	.21	-.05
sf11c	"Expect my health to get worse"		.21	-.05	.00	-.06	.04	.15
sf11d	"Health is excellent"		**.47**	-.12	-.09	.06	.15	.08
sf9a	"Felt full of life"	VT	**.32**	-.09	.09	-.09	.07	.26
sf9e	"Have had a lot of energy"		.28	-.06	.07	-.01	.12	**.40**
sf9g	"Felt worn out"		-.07	.05	-.09	.10	.15	**.79**
sf9i	"Felt tired"		-.11	.06	.00	-.01	.06	**.89**
sf6	"Extent physical health or emotional problems interfered with normal social activities"	SF	.02	.04	.03	.03	**.80**	-.03
sf10	"Physical health or emotional problems have interfered with social activities"		.07	.06	.06	.02	**.76**	-.06
sf5a	"Due to emotional problems cut time on work"	RE	-.01	.05	**.61**	.01	**.33**	-.08
sf5b	"Due to emotional problems accomplished less"		-.04	.03	**.82**	.00	.14	.02
sf5c	"Due to emotional problems work less carefully"		.01	.01	**.63**	.00	.20	-.06
sf9b	"Been very nervous"	MH	-.16	.09	.07	-.05	**.69**	.09
sf9c	"Felt so down in dumps"		-.07	-.02	-.07	.01	**.91**	-.03
sf9d	"Felt calm and peaceful"		.03	-.02	.12	-.09	**.67**	.03
sf9f	"Felt downhearted and low"		-.10	-.05	-.09	-.04	**.86**	.13
sf9h	"Been happy"		.15	-.14	.09	-.06	**.53**	.08

PF=physical functioning, RP=role physical, BP=bodily pain, GH=general health, VT=vitality, RE=role emotional, SF=social functioning, MH=mental health

Table 6. Rotated structure in a two-component PCA. Presenting item loads on component 1 and 2. Items with loadings ≥ 0.32 are marked in boldface. (paper III)

Items	Item text	Composite scores	Component 1	Component 2
sf3a	"Health limits vigorous activities"	Physical dimension	**.40**	-.01
sf3b	"Health limits moderate activities"		**.76**	.00
sf3c	"Health limits lifting and carrying groceries"		**.62**	-.07
sf3d	"Health limits climbing several flights of stairs"		**.70**	-.05
sf3e	"Health limits climbing one flight of stairs "		**.75**	-.14
sf3f	"Health limits bending, kneeling or stooping"		**.70**	-.07
sf3g	"Health limits walking more than a mile"		**.78**	-.14
sf3h	"Health limits walking several hundred yards"		**.82**	-.17
sf3i	"Health limits walking one hundred yards "		**.71**	-.21
sf3j	"Health limits bathing or dressing yourself "		**.55**	-.05
sf4a	"Due to physical health cut down time on work"		**.47**	.23
sf4b	"Due to physical health accomplished less"		**.45**	.24
sf4c	"Due to physical health limited in work"		**.60**	.08
sf4d	"Due to phys. health difficulty perform. work"		**.61**	.11
sf7	"Bodily pain"		**.51**	.13
sf8	"Pain interfered with normal work"		**.57**	.21
sf1	"Self reported health"		**.55**	.18
sf11a	"Seem to get ill more easily than other people"		.14	**.32**
sf11b	"As healthy as anyone I know "		.28	.26
sf11c	"Expect my health to get worse"		.09	.18
sf11d	"Health is excellent "		**.32**	.28
sf9a	"Felt full of life"		.11	**.38**
sf9e	"Have had a lot of energy"	Mental dimension	.16	**.51**
sf9g	"Felt worn out"		.09	**.57**
sf9i	"Felt tired"		.01	**.57**
sf6	"Extent physical health or emotional problems interfered with normal social activities"		.03	**.79**
sf10	"Physical health or emotional problems have interfered with social activities"		.08	**.76**
sf5a	"Due to emotional problems cut time on work"		-.01	**.67**
sf5b	"Due to emotional problems accomplished less"		-.06	**.68**
sf5c	"Due to emotional problems work less carefully"		-.04	**.59**
sf9b	"Been very nervous"		-.11	**.72**
sf9c	"Felt so down in dumps"		-.10	**.82**
sf9d	"Felt calm and peaceful"		-.10	**.78**
sf9f	"Felt downhearted and low "		-.17	**.86**
sf9h	"Been happy "		-.09	**.73**

5. Discussion

5.1 Methodological issues

5.1.1 Study designs, patients and representativity

In all the studies (paper I-III) the subjects were Norwegians of Europoid origin, meaning that the results cannot be generalized to other populations.

Paper I and II

The MOBIL study was designed as a pragmatic non-randomised clinical trial aiming to compare the effectiveness of RYGB and ILI when performed in tertiary care centres, specialised in the treatment of morbidly obese patients. The term "pragmatic" is used to describe trials designed to help choose between options for care. Its counterpart "explanatory" describes trials designed to test causal research hypotheses, eg. that an intervention causes a particular biological change [152]. The pragmatic design is considered more relevant for clinical work and may guide clinical decisions more directly than studies with an explanatory design [152].

When planning the study, RYGB was thought to be more effective than ILI at reducing weight and improving co-morbidities [110]. According to Norwegian guidelines, treatment seeking morbidly obese subjects should be offered either conservative or surgical therapy [153]. We therefore considered it unethical to randomly assign patients to RYGB if they qualified for an ILI and vice versa. However, this stance has met criticism. When the sample was not randomised, baseline differences may give room for confounders and selection bias, thereby obscuring the assessment of effectiveness of the two treatments. Compared to the ILI group, the patients in the RYGB group had a higher BMI, were younger, had earlier onset of obesity, and had lower physical and emotional HRQL. Expecting possible baseline

differences between groups [41, 154], multiple regression analyses were planned and performed (both in paper I and paper II) in order to adjust for and minimize the possible confounding effect of such differences.

Paper III

This cross-sectional validation study was based on data collected at a Norwegian rehabilitation centre specializing in treating morbidly obese patients. The sample in paper III consisted solely of treatment seeking morbidly obese subjects. Morbidly obese persons seeking treatment may have greater psychological stress than non-treatment seeking severely obese [32]. Consequently, generalizability to the general morbidly obese population may be limited. Nevertheless, as the prevalence of morbid obesity has increased dramatically over the last decade, it is to be expected that larger numbers of morbidly obese may wish to receive treatment, diminishing the potential discrepancy between sample results and population. Furthermore, morbidly obese choosing lifestyle intervention or bariatric surgery differ in terms of BMI, age, obesity history and HRQL [41, 154], and as such, the results from the validation study presented in paper III cannot directly be generalized to morbidly obese not seeking bariatric surgery.

5.1.2 Data quality

As described earlier, all anthropometric measurements were performed in a standard manner. Some of the explanatory variables (eg. work status, marital status, age at onset of obesity, length of education, and physical activity) were registered through interviews by internists, nurses and registered dieticians. The accuracy of such information is dependent on the patients' motivation and memory. There is evidence that obese patients tend to overestimate physical activity [155, 156]. Such data may then not be as accurate as if energy expenditure

was measured by indirect or direct calorimetry or by a number of non-calorimetric techniques (predicting energy expenditure by extrapolating from physiological measurements). Patient registration of HRQL may also be affected by motivation. If a patient was to register his or hers HRQL prior to a treatment decision, and in order to be prioritized, the patient would perhaps register a worse HRQL score than if treatment had already been decided upon. In the studies forming this thesis, registration of HRQL data was performed after study inclusion in the study. The SF-36 has a 1-week recall and the questions aim to elicit answers related to HRQL elements as they have been over the last week. The other questionnaires aim to explore the "current" situation of patients.

5.1.3 Missing data

Missing data is common in HRQL research and is a methodological obstacle since it represents a risk of biased estimates, distorted statistical power and invalid conclusions [145].

Missing data in paper II was dealt with by multiple imputations of missing values, whilst in in paper I and III with mean imputation. We applied also the full information maximum likelihood (FIML) method in paper III.

Multiple imputation is based on a prediction model containing variables theoretically associated with the variables with missing values. The missing values are predicted using existing values from other variables. We created 20 data sets; even if a smaller number of data sets has been suggested as valid [157]. However, as the missing data in the 1 year data set for some variables was over 20%, 20 datasets with 10 iterations per dataset were needed to give an expected relative efficiency of 98-99% [157-160]. Standard statistical analyses were carried out on each imputed data set, producing multiple analyses results. These analyses results were then combined to produce one overall (pooled) result [159-161]. Multiple

imputation accounts for missing data by restoring not only the natural variability in the missing data, but also by incorporating the uncertainty caused by estimating missing data. The missing values accounted for in paper II may produce a risk of biased estimates, but when handled by multiple imputation, this risk was considerably reduced [161].

Of the 537 patients in paper III, 62 (11%) had more than 60% missing item values, thereby reducing the accuracy of multiple imputation techniques [159-161] and leaving 475 (89%) patients eligible for further statistical analysis. Missing data in the remaining sample (n=475) were handled through mean imputation prior to the PCA. Mean imputation is the replacement of a missing observation with the mean of the non-missing observations for that variable. This method has been questioned [145] even though it may accurately predict missing data, especially when missing values are missing completely at random. Even though the missing values was missing completely at random, mean imputation may, theoretically have affected the result of the PCA that rely heavily on the correlation mathematics and variance-covariance matrixes. However, in paper III we applied structural equation modelling to perform confirmatory analyses. When applying structural equation modelling the FIML method is available. This missing imputation method uses the whole dataset and, by using maximum likelihood estimation, missing values are calculated and imputed. FIML is considered the gold standard for the handling of missing data as it applies a full dataset to calculate the probability of the correct values in the missing data [160, 161]. The structural equation modelling results corresponded with the results of the PCA, giving support for the accuracy of the mean imputation of missing data in the PCA-analyses.

5.1.4 Other methodological considerations

Assessment of clinical relevance

For many clinicians, the unfamiliarity with the many available HRQL instruments may lead to research findings that are difficult to interpret in a clinical setting. To reduce this potential problem, other methods for assessing HRQL-changes have been developed and applied [142-144, 163-166]. The calculation of Cohens *d*, as performed in paper II, is commonly used. There are however alternative distributional approaches [144].

The distributional approach aims to measure the reliability of the change score. A recommended method is to calculate the standard error of measurement (SEM). The SEM is calculated [144] as the standard deviation of the score multiplied by the square root of 1 minus the reliability of the scale (eg. Cronbach's alpha coefficient).

Even though several studies have shown the usefulness in applying SEM calculations, there is still no agreement as to how large the SEM-change should be in order to detect a clinical relevant change in an individual [166]. Some studies find a close correspondence between a 1 SEM change and a minimally detectable difference in clinical anchors [167, 168], whilst others finds such correspondence with larger estimates [169], especially in HRQL-instruments. A 1 SEM change approximates a 68% confidence interval based on a standard normal curve. Norquist et. al. [166] suggest an estimate of 1.96 * SEM, which approximates a 95% confidence interval as a conservative approach to reduce the risk of chance.

The standard error of difference (S_{diff}) [166] between two time points is calculated as the square root of the subtraction between the SEM at time 1 and SEM at time 2 [168].

We have performed post- hoc calculations of SEM and S_{diff} based on the data presented in paper II. SEM was calculated at baseline and 1 year on each of the 5 HRQL-dimensions. The SEM-values were multiplied with 1.96 to approximate the 95% confidence interval and the S_{diff} between baseline and 1 year was calculated for each of the HRQL dimensions.

As shown in table 7, the S_{diff} indicates that a reliable change in the physical dimension should be higher than 12 points. A reliable change on the mental dimension should be higher than 13 points, whilst on the emotional dimension such a change should be higher than 14 points. Likewise, the number of symptoms should be reduced by 5 and the symptom distress should be reduced by 20 points.

Table 7. Baseline scores and Cronbach's alpha coefficients at baseline and one year. Standard error of measurement (SEM) and standard error of difference (S_{diff}) at 1 year. Morbidly obese patients (n=139)

	Baseline			One year			1.96*SEM		
	Mean	(SD)	α	Mean	(SD)	α	Baseline	One Year	S_{diff}
Physical dimension	36,1	(10,5)	0,82	47,5	(10,3)	0,81	8,71	8,71	12,31
Mental dimension	41,1	(10,8)	0,81	47,9	(10,1)	0,79	9,28	9,16	13,03
Emotional dimension	35,7	(23,7)	0,95	66,1	(26,5)	0,96	10,39	9,85	14,32
Number of symptoms	11,2	(4,1)	0,82	7,1	(4,8)	0,84	3,42	3,72	5,05
Symptom pressure	40,5	(21,0)	0,86	20,2	(16,6)	0,85	15,18	12,43	19,62

The majority of patients in the RYGB group report reaching clinical relevant results on physical HRQL, emotional HRQL and symptom distress (table 8). The majority of patients in the ILI group reached clinical relevant results on emotional HRQL only. The improvement of the emotional HRQL in the RYGB group was particularly pronounced and 87% of the patients in the RYGB group reached clinical relevant results after one year (change score > 14 points).

The lifestyle group also reported significant improvements in the emotional dimension of HRQL after one year, with 52% reaching clinically relevant results. Only 47% of the patients in the RYGB group and 27% of the patients in the ILI group reported > 5 symptoms reduction after one year. As with the emotional and physical aspects of HRQL, the mental aspects of HRQL also improved in both groups after 12 months, even though only 32% and 14% in the RYGB-group and lifestyle-group reached clinical relevance.

Table 8. Number (%) of patients reaching reliable HRQL change. RYGB (n=76) and ILI (n=63).

	RYGB		ILI		
	N	%	n	%	p-value
Physical HRQL	48	63.2	13	20.6	<.001
Mental HRQL	24	31.6	9	14.3	.005
Emotional HRQL	66	86.8	33	52.4	<.001
Number of symptoms	36	47.4	17	27.0	.027
Symptom distress	46	60.5	21	33.3	.004

Weight loss or treatment choice as explanatory variable (paper II)

Weight loss and improvement of HRQL are significantly associated [37, 110, 170-176]. When performing the multivariate regression analyses (ANCOVA) on the 5 HRQL scales (table 3) the degree of weight change would normally have been incorporated in the regression model. However, weight loss and intervention method were highly correlated (r = .81). The mean (SD) 1-year weight loss in the RYGB group was 30 (8) % of initial body weight and 8 (9) % in the ILI group [140], with all patients in the RYGB group losing more than 15% of their baseline weight. In the ILI group 62% lost ≥ 5% and 38% lost ≥ 10% of their baseline weight.

If the two highly correlated variables (weight loss and intervention method) were to be analysed in the same models, the standard errors of both standardized and unstandardized

coefficients would inflate and obscure the interpretation of the analyses [145]. Several methods were tested: building indexes (combining treatment and weight loss), centring the weight loss variable on its mean, as well as re-specifying the regression model and entering an interaction term as the cross product of the two variables. We decided, however, to implement the most common procedure, that is, the removing of the intercorrelated variable (weight loss) from the analyses. Being aware of the strong association between weight loss and increased HRQL in morbidly obese patients, we ran separate linear multivariate regression analyses with weight loss in the multivariate models (instead of treatment). The linear regression analyses revealed significant associations between weight reduction in percent of baseline weight, when controlling for the effect of gender, age at baseline, age at the onset of obesity, BMI at baseline and physical activity at baseline. The analyses showed consistent significant associations between weight loss and HRQL change, after controlling for potential covariates.

5.2 Main findings and discussion

5.2.1 The importance of employment

Being employed imparts greater benefits than purely financial stability; it implies also that important routines are formed in daily life and that human contact and social bonds with colleagues are formed. In our study (paper 1) we found that employment was associated with increased physical and mental HRQL when compared to unemployed patients. However, employees did not report a better emotional HRQL than those who were unemployed. One possible explanation for this is the phenomenon of stigma [74-86, 96, 177], as was discussed earlier in this thesis. Being employed implies socializing with colleagues and conforming to the norms of the workplace, but at the same time the norms of society at large still prevail. If the strong connections between general anti-fat attitudes, stigma and negative emotional HRQL hold water, it is then of no surprise that employment does not have a significant impact

on emotional HRQL. Women had a lower emotional HRQL independent of whether they were employed or not. This finding is in accordance with a Swedish study [83] reporting that severely obese women experienced workplace discrimination to a greater extent than obese men and normal weight women.

Physical HRQL was higher in the employed group of morbidly obese than the unemployed group. This association was independent of age, gender, obesity history, BMI, sedentary lifestyle, marital status, and comorbidities such as hypertension, type 2 diabetes and obstructive sleep apnoea. One explanation is that employment itself has a positive effect on physical HRQL and that this effect is prominent even when controlling for comorbidities such as gender, age, education and marital status. Being employed implies having routine such as waking up at regular times, travelling to work, walking around the workplace, walking up stairs and so on, thereby strengthening physical functioning and reducing physical role limitations.

The finding of a positive association between work status and HRQL may also be interpreted as a "healthy worker effect". Occupational groups often have fewer illnesses and disabilities and they are more likely to be assessed as healthier than the population as a whole, giving rise to both selection and confounding bias [178, 179]. There are many possible explanations of this "healthy worker effect" but the two main explanations are the "healthy hire effect" and "the healthy worker survivor effect". The former suggests that the healthiest (unhealthy) persons are (not) selected to the workforce. The latter suggests that the most healthy workers stay in those very same jobs [179]. It may be hypothesized that morbidly obese patients with impaired HRQL also have various levels of disability, and were either not selected into the workforce in the first place ("healthy hire effect") and/or that patients with low HRQL could not retain their positions ("healthy worker survivor effect") [179].

In sum, the findings in paper I (as in other studies of employment and HRQL) could be influenced by both systematic selection and confounding bias. However, the cross-sectional study design does not infer any causal relationship and such interpretations cannot be verified.

5.2.2 Lifestyle interventions

The ILI at the heart of paper II consisted of 4 stays totalling 7 weeks. The patients improved their HRQL across all dimensions and especially in terms of emotional HRQL, although the average weight loss was moderate (8% of baseline weight). Thus, weight loss may not be the only explanation of elevated HRQL scores in the ILI group. It is conceivable that the intervention itself contributed to this improvement. The group-based focus and motivational approach of the lifestyle programme aimed at increasing self-efficacy, self-esteem and mood state. Previous studies seem to support this idea. Programmes focusing on motivationally-oriented group sessions report as little as 3 kg. weight loss (e.g. from 103 to 100 kg.), but have found significant improvements in mood state as measured with validated psychometric instruments [180]. In another study of 440 obese patients with coronary artery disease, group support was reported to be associated with a significant improvement in the mental dimension of HRQL despite moderate weight loss [181].

An interesting finding in the MOBIL-study discussed in paper II was a greater overall increase in the physical activity level of the ILI group compared to that of the RYGB group ($p = .022$) [140, 182]. Changes in physical activity were not connected to changes in HRQL in our study. Reviews and meta-analyses of the scientific literature have shown significant associations in other studies between increasing levels of physical activity and improved HRQL in the general population [183, 184] and in morbid obesity [185], albeit that there are few randomised trials testing the effect of physical activity on HRQL in morbid obesity. In a randomised trial of sedentary, overweight and obese (BMI range 25-43 kg/m^2)

postmenopausal women with elevated systolic blood pressure, physical activity improved physical and mental HRQL in a dose-dependent fashion, whilst the improvements in HRQL were independent of weight loss [131].

5.2.3 Validation of SF 36

Our validation of this instrument questions the structural validity of the subscale scores. However, our results do not dissuade the use of SF-36 in studies of morbid obesity, but there are some important considerations and limitations to the use of SF-36 as an outcome measure in this population. Firstly, the clinical interpretation of the subscale scores is obscured due to ambiguity regarding their meaning. Researchers utilizing the SF-36 subscales should be aware of this and use obesity-specific HRQL instruments as supplementary measures. The subscale scores of the SF-36 will probably be more adequately interpreted when compared to such diagnosis-specific instruments. Secondly, despite the high validity of the summary scales, there are disadvantages to using them at the expense of the subscales. The most important is related to the loss of information. The 'physical summary scale' consists of 21 items and the 'mental summary scale' of 14 items. Consequently, a lot of detailed information is lost. Another disadvantage of using the summary scales is related to the scoring algorithm. Some authors claim that the scoring algorithm, which is based on an orthogonal factor score, not accounting the high correlation between the two, produce unreliable results [58, 59]. The scale authors argue as a response that the scoring algorithm is for all practical purposes reasonable [60]. Again, other authors propose to adjust the scoring algorithm by using oblique factor rotations in the scoring algorithm [61]. As a consequence of this discourse, researchers planning to use the summary scales in the study of obesity should examine the literature on which algorithm to use and comment on their choice.

6. Possible implications for practice

We have shown that employment is positively associated with HRQL in morbidly obese. As shown in paper I, one third of treatment seeking morbidly obese patients receive disability pensions. Clinicians should discuss the important association between employment and HRQL with their patients before suggesting disability pension.

We have also shown that after 1 year RYGB is a more effective improver of HRQL than ILI. Our findings also indicate that a comprehensive ILI program focusing on physical activity, meal reduction and behavioural change was able to induce improvements in most HRQL dimensions. Long term studies of bariatric surgery like the Swedish SOS-study [109, 110] have shown increasing weight and decreasing HRQL amongst bariatric patients over time, underscoring the importance of lifestyle change. Clinicians should emphasise to patients that bariatric surgery is primarily a means of achieving lifestyle change rather than a "final solution" for obesity. Given the promising results of the ILI, bariatric patients regaining weight should be referred to intensive lifestyle treatments.

RYGB is associated with a wide range of complications [111-114], with patients most likely having to take dietary supplements for the rest of their lives. Given the very low complication rate following ILI, RYGB may not, despite its ability to improve HRQL and risk factors [140], be *the* primary option. Clinicians should discuss the possible complications of RYGB with their patients and should consider ILI as an alternative to RYGB.

7. Implications for further research

The prevalence of adult individuals with BMI ≥ 40 kg/m^2 in Norway is estimated to be 5% in men and 1.5% in women [11]. It is obvious that research should focus on obesity prevention methods, especially those aiming to help children and adolescents. For society at large, public health research should aim to evaluate initiatives which hinder the expansion of obesogenic structures in our culture.

However, we also need research focusing on different treatment alternatives for those in need of treatment. Unlike bariatric surgery, where RYGB is considered a "gold standard" [103], no similar recommendation exists in terms of ILI. We need well designed controlled randomised studies comparing the effects of different ILI's on HRQL and other parameters like weight loss, physical fitness and comorbidities. We also need studies which evaluate the long-term effect of ILI's on HRQL.

The design of more effective lifestyle programs aiming at the improvement of patient HRQL is important. Several studies [124, 131, 137-139, 180, 181, 183-185] indicate that an expansion of the ILI's program mode, both in terms of its content (eg. physical activity, nutrition and behavioural focus) and length will give more positive results, both in terms of HRQL but also in terms of weight loss.

In sum, psychosocially oriented ILI's which aim to increase physical activity and eating patterns through behavioural change are promising. However, conservative treatment programs for the morbidly obese are relatively new. Systematic evaluations of different programs are still needed in order to develop more effective ILI's.

Studies of ILI should also explore the economic costs of the treatment in order to develop more cost-effective treatments. Cost is an important factor given that the aim is to help as many morbidly obese individuals as possible.

8. General conclusions

We conclude that employed morbidly obese subjects have higher HRQL than their unemployed peers. Employment was independently associated with both the physical and mental dimensions of HRQL, controlling for age, gender, current BMI, obesity history, marital status and comorbidities. Conversely, gender (and not employment) was associated with the emotional dimension of HRQL.

We can also conclude that morbidly obese patients following a part residential multidisciplinary lifestyle intervention program improved their HRQL, although patients undergoing bariatric surgery experienced larger improvements in HRQL after 1 year. The higher clinical relevance of bariatric surgery in terms of HRQL may be explained by a higher weight loss.

Finally, we conclude that when measuring HRQL, the summary scales of the SF-36 have satisfactory construct validity in patients with morbid obesity, although the subscale scores should be interpreted with care. The summary scales of the SF-36 may be considered the primary scales when assessing HRQL in morbidly obese patients initiating lifestyle treatment.

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Paper I

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CLINICAL RESEARCH

Employment Is Associated with the Health-Related Quality of Life of Morbidly Obese Persons

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Abstract
Background We aimed to investigate whether employment status was associated with health-related quality of life (HRQoL) in a population of morbidly obese subjects.
Methods A total of 143 treatment-seeking morbidly obese patients completed the Medical Outcome Study 36-Item Short-Form Health Survey (SF-36) and the Obesity and Weight-Loss Quality of Life (OWLQOL) questionnaires. The former (SF-36) is a generic measure of physical and mental health status and the latter (OWLQOL) an obesity-specific measure of emotional status. Multiple linear regression analyses included various measures of the HRQoL as dependent variables and employment status, education, marital status, gender, age, body mass index (BMI), type 2 diabetes, hypertension, obstructive sleep apnea, and treatment choice as independent variables.
Results The patients (74% women, 56% employed) had a mean (SD, range) age of 44 (11, 19–66) years and a mean BMI of 44.3 (5.4) kg/m^2. The employed patients reported significantly higher HRQoL scores within all eight subscales of SF-36, while the OWLQOL scores were comparable between the two groups. Multiple linear regression confirmed that employment was a strong independent predictor of HRQoL according to the SF-36. Based on part correlation coefficients, employment explained 16% of the variation in the physical and 9% in the mental component summaries of SF-36, while gender explained 22% of the variation in the OWLQOL scores.
Conclusion Employment is associated with the physical and mental HRQoL of morbidly obese subjects, but is not associated with the emotional aspects of quality of life.

Keywords Employment · Obesity · Health-related quality of life

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Introduction

Health-related quality of life (HRQoL) refers to the impact of a medical condition on the physical, social, and emotional functioning reported by a respondent. HRQoL is often assessed by standardized questionnaires, the generic SF-36 being the most commonly used [1]. Several lines of evidence indicate that there is a relationship between increasing levels of obesity and impaired HRQoL [2, 3], the latter of which has been shown to improve after bariatric surgery [4, 5].

A number of studies have addressed the relationship between socioeconomic factors and the impaired HRQoL of obese persons, with at least three finding significant associations between marital status, income, education, and the HRQoL [6–8]. There is also some evidence to suggest that obesity-related comorbidities and conditions such as hypertension and type 2 diabetes may influence HRQoL in morbidly obese women and men [3, 7, 8]. However, previous studies have taken into account only a limited

number of comorbidities and have done so with variable diagnostic precision. Some of these studies are devoid of socioeconomic considerations in their analyses.

Morbidly obese women have been found to have lower HRQoL than men, particularly in terms of the impairment of physical function and body image/body satisfaction [9–11]. In addition, white subjects would seem to have lower quality of life than other ethnic groups [10, 11]. Finally, morbidly obese patients seeking surgery have been shown to have lower HRQoL than those who do not [12].

A study of 51 morbidly obese subjects treated with duodenal switch [6] demonstrated a statistically significant association between employment and the physical and mental component scores of the SF-36. The study was, however, limited by lack of adjustments for obesity-related comorbidities and conditions which might have influenced HRQoL. In addition, no obesity-specific measure of quality of life was addressed.

We aimed to investigate whether the general and obesity-specific HRQoL of treatment-seeking morbidly obese Caucasian subjects were associated with employment status after adjustments for confounding factors.

Materials and Methods

Study Design and Participants

The non-randomized controlled MOBIL study (Morbid Obesity treatment, Bariatric surgery versus Intense Lifestyle intervention, Clinical Trials.gov number NCT00273104) was designed to compare the effects of bariatric surgery and intensive lifestyle intervention on various comorbidities, eating behavior, and quality of life [13]. In the present cross-sectional study, 145 patients were asked to complete two questionnaires related to HRQoL at baseline. Two patients did not complete the questionnaires, and as such, data from 143 morbidly obese subjects, all but one Caucasian, was included in the analysis.

The regional Ethics Committee for Medical Research approved the study protocol, and the study was performed in accordance with the Declaration of Helsinki. All participants gave informed written consent before enrolment. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research.

Outcomes, Explanatory Variables, and Potential Confounders

The main outcome was HRQoL as measured by various questionnaires exploring the physical, mental, and emotional aspects. The main explanatory variable was employment status, with possible confounders adjusted for including socioeconomic factors, age, gender, body mass index (BMI), obesity-related comorbidities, and treatment-seeking status. Persons receiving income from either full-time or part-time work were defined as employed.

HRQoL

Two different questionnaires were used to measure HRQoL: the Medical Outcome Study 36-Item Short-Form Health Survey (SF-36) and the Obesity and Weight-Loss Quality of Life (OWLQOL). SF-36 is a commonly used generic measure of health status based on a comprehensive set of items. It has eight subscales (physical function, role physical, bodily pain, general health, role emotional, social function, vitality, and mental health), which generate two general health summaries: the physical and mental component scores [14, 15]. The OWLQOL primarily measures the emotions and feelings which result from being obese and trying to lose weight. The instrument consists of 17 statements about weight and quality of life. All items are rated on a seven-point scale from 0 (not at all) to 6 (a lot), with lower scores better than higher. The OWLQOL scale is adjusted to 0–100 (higher = better) after reversing the scores. The OWLQOL was originally produced at the University of Washington and has been further developed through input from five European countries and the USA. The questions have been translated into Norwegian and are available with permission from the Seattle Quality of Life Group, University of Washington [16, 17].

Clinical Examination

All participants underwent a medical examination by a physician during their first consultation. Demographic data, socioeconomic history, and medical history were recorded using standardized schemes. Weight and height were measured with patients wearing light clothing and no shoes. BMI was calculated as weight in kilograms divided by the square of the height in meters. Blood pressure was measured three times after at least 5 min rest, at the right or left brachial artery, with the patient in a sitting position. The average of the second and third measurements was registered. Hypertension was confirmed if either systolic blood pressure was greater than 140 mmHg, if diastolic blood pressure was greater than 90 mmHg, or if the patient received antihypertensive drugs.

All patients underwent one overnight sleep with a portable monitor, the Embletta™ system; which has both high sensitivity and specificity when compared to the “gold standard” overnight polysomnography used to identify obstructive sleep apnea (OSA) patients [18]. OSA was diagnosed in patients having moderate to severe sleep

apnea (apnea–hypopnea index (AHI)≥15 events per hour) as these patients are more likely to have symptoms than those with mild OSA.

Type 2 diabetes was diagnosed in patients either treated with glucose-lowering drugs or with a fasting serum glucose ≥7.0 mmol/l and/or a 2-h glucose ≥11.1 mmol/l after the ingestion of a 75-g anhydrous glucose solution [13].

In addition, all patients completed a questionnaire on their diet and physical activity [19]. Patients were categorized as having a sedentary lifestyle if they had no (less than 10 min a week) aerobic moderate or vigorous activity based on their answer to the following question: "Do you perform any physical activity and exercise making you a little short of breath (more than 10 min a week bicycling, swimming, walking, skiing, dancing, or golfing)?"

Statistical Analysis

Data are presented as mean (SD) or *n* (percent) unless otherwise stated. The reliability of the HRQoL scales was assessed with inter-item analysis using Chronbach's alpha. The scales were examined for normality using skewness tests and Kolmogorov–Smirnov testing. None of the scales had significant departures from normality. The continuous independent variables underwent the same normality testing and neither was found to have significant departures from normality.

Between group comparisons were analyzed using independent samples *t* test and χ^2. The correlation between each of the independent and the dependent variables was calculated using Pearson correlation coefficient. We also performed three multiple linear regression analyses, one for each scale as the dependent variable. Ten predefined explanatory variables were included in each model. In examining the variation of inflation factors in the models, we found no consequential multicollinearity between the independent variables. The probability–probability plot between expected and observed cumulative distribution was considered acceptable. Semi-partial (part) correlation coefficients were squared in order to calculate the percentage of total variance in the dependent variable explained by a given independent variable. Throughout, we report two-tailed *P* values, as we considered values below .05 to be statistically significant. Particular attention should, however, be directed towards small *P* values, e.g., those below .01, because a considerable number of *P* values have been calculated. The statistical analysis was conducted using SPSS v.17.0.

Results

The reliability of the scales as measured by the Chronbach's alpha was 0.93 for the SF-36 and 0.95 for the OWLQOL. Table 1 shows demographic, socioeconomic, and clinical characteristics according to employment status. The 143 morbidly obese patients (74% women) had a mean (SD, range) age of 44 (11, 19–66) years and a mean BMI of 44.3 (5.4) kg/m^2. The employment rate was 56%. The employed and unemployed groups were comparable with respect to age, gender, BMI, sedentary lifestyle, and obesity-related comorbidities (Table 1).

Nearly all of the unemployed patients (91%) received benefits from the state, including disability benefits (38%), rehabilitation benefits (24%), sick leave (16%), unemployment benefits (5%), retirement pensions (5%), and unknown (3%). The unemployed group had a significantly lower average level of education and tended to opt for bariatric surgery more often than their employed counterparts (Table 1).

The physical and mental scores of SF-36 were significantly higher in the employed group than the unemployed group (Table 1). The emotional aspects of quality of life as measured with the OWLQOL did not differ between the two groups (*P*=.86).

Differences between the employed and the unemployed groups within the various subscales of SF-36 are shown in Fig. 1. The employed patients reported significantly higher HRQoL within all eight subscales; this was most pronounced within the physical function, role physical, bodily pain, and role emotional subscales.

The multiple linear regression models (Table 2) confirmed that employment was significantly associated with higher scores for general physical and mental health according to both SF-36 dimensions after adjustment for confounding factors. In contrast, only gender was significantly associated with the emotional aspects of obesity as measured by the OWLQOL (women had lower scores than men). Neither age, level of obesity, comorbidities, nor education were significantly associated with HRQoL.

Squared part correlations showed that employment explained 16% of the variation in the physical component score of the SF-36 and 9% of the variation in the mental component score of the SF-36. Gender explained 22% of the variation in the OWLQOL scores.

Discussion

Our study demonstrates that in morbidly obese patients allocated to either surgical treatment or lifestyle intervention, employment was independently associated with both the physical and mental aspects of HRQoL. Conversely, employment was not associated with the emotional aspects of quality of life.

Table 1 Demographic, socio-economic, and clinical characteristics among 143 morbidly obese subjects according to employment

Variable	Total	Employed (n=80)	Unemployed (n=63)	P value
Age (years)	44.6 (10.7)	44.1 (10.2)	45.2 (11.3)	0.557
Women	106 (74%)	63 (79%)	43 (68%)	0.180
Start obesity				
<12 years	34 (25%)	22 (28%)	12 (20%)	
12–20 years	32 (23%)	14 (18%)	18 (30%)	
>20 years	72 (52%)	42 (54%)	30 (50%)	0.207
BMI (kg/m^2)	44.3 (5.4)	43.7 (5.6)	45.0 (5.2)	0.180
Current smoker (yes)	38 (27%)	19 (24%)	19 (31%)	0.445
Sedentary lifestyle (yes)	36 (31%)	21 (33%)	15 (28%)	0.689
Socioeconomic factors				
Married/cohabitant (yes)	89 (62%)	54 (68%)	35 (56%)	0.166
Length of education				
Basic (<9 years)	35 (25%)	9 (11%)	26 (42%)	
Intermediate (9–12 years)	72 (51%)	49 (61%)	23 (38%)	
Higher (>12 years)	34 (24%)	22 (28%)	12 (20%)	<0.001
Comorbidities				
Hypertension (yes)	52 (36%)	28 (35%)	24 (38%)	0.729
Type 2 diabetes (yes)	44 (31%)	24 (30%)	20 (32%)	0.855
OSA (AHI ≥15; yes)	43 (31%)	21 (27%)	22 (37%)	0.267
Seeking surgery (yes)	84 (59%)	41 (51%)	43 (68%)	0.059
Quality of life				
SF-36 physical	46 (24)	55 (22)	33 (20)	<0.001
SF-36 mental	55 (25)	62 (23)	47 (24)	0.001
OWLQOL emotional	35 (24)	35 (23)	35 (25)	0.864

Data are given as mean (SD) or number (percent). P values were calculated using independent samples t test or χ^2

Employment

Our study confirms the findings of previous studies which demonstrated a relationship between participation in paid work and general HRQoL in patients undergoing bariatric surgery [6, 20]. Through our study, we are able to both extend this association to a sample of morbidly obese subjects offered either conservative or surgical treatment and to suggest that it is valid independent of confounding factors. However, we found no association between the emotional aspects of quality of life and employment status.

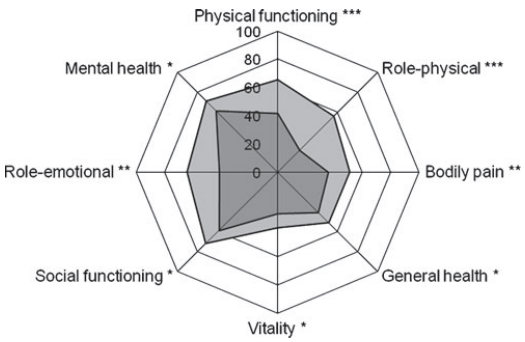

Fig. 1 The SF-36 subscale mean scores among employed and unemployed patients. The SF-36 subscales differed significantly between employed (*light grey*) and unemployed (*dark grey*) patients. Independent samples t test; *** p<0.001, **p<0.01, *p<0.05

Our findings are also in accordance with a previous study of patients with inflammatory bowel disease, which showed that employment was associated with HRQoL as measured by SF-36 [21]. It could be argued that employed patients use their physical and mental capacities and might therefore pay less attention to any general health limitations and discomfort they may have. Employment might give both a sense of inclusion and belonging, providing patients with access to both working and social networks. This hypothesis is supported by studies of both cancer patients and older adults which have shown positive associations between social networks, support, and HRQoL [22, 23]. Employment may also positively contribute to a person's self-esteem. Nevertheless, in the present study, emotional QoL was comparable among both employed and unemployed patients, indicating that participation in paid work does not seem to relieve the emotional distress of being morbidly obese [24].

Table 2 Predictors of HRQoL in 144 morbidly obese patients

QOL dimension	Physical, R^2=0.36, beta	Mental, R^2=0.17, beta	Emotional, R^2=0.26, beta
Gender	0.13	0.15	0.51***
Age	−0.22*	0.07	0.07
BMI	−0.09	0.13	−0.15
Marital status	−0.09	−0.02	0.05
Education	−0.07	−0.06	0.01
Employment	0.43***	0.33**	0.07
Hypertension	0.03	0.01	0.16
OSA	−0.09	−0.03	0.06
Type 2 diabetes	−0.14	−0.11	−0.04
Seeking surgery	0.26**	0.12	0.13

The main explanatory variable was employment status, with possible confounders adjusted for including other socioeconomic factors, age, gender, BMI, obesity-related comorbidities, and treatment-seeking status. Standardized beta values are given

*P<0.05; **P<0.01; ***P<0.001 (linear regression)

The employment rate among the patients was 56%, while the overall Norwegian employment rate at the same time of the study was 73% [25]. A large proportion of the jobs patients held were within low wage service sectors like transport, accommodation, and food and health (data not shown). The Norwegian welfare system provides a significant range of benefits for persons without work. We therefore believe that poverty plays a minor role in explaining why unemployed morbidly obese patients reported impaired HRQoL.

Gender

The general physical and mental HRQoL scores were nearly equal between the morbidly obese men and women in the study. However, the obesity-specific emotional measurement OWLQOL showed that women reported significantly more concerns about emotional and social distress. Previous studies have demonstrated impaired HRQoL among morbidly obese women [9, 10]. Some authors have also suggested there to be less social obesity stigmatization among African American women [11]. Our study confirms that for white females, obesity has a stronger effect upon the emotional quality of life than the general HRQoL. The question whether this finding is also valid for women of other ethnicities should be addressed in future studies.

Comorbidities

We found no statistically significant associations between weight-related comorbidities and quality of life. This finding concurs with at least one previous study [3]. Most patients had either no symptoms or only mild symptoms as a result of the comorbidities and did not seem to be very bothered by these. Many of them were not even aware of their comorbidity before the study examination. Thus, it seemed that being unemployed overshadowed the potential problems following hypertension, obstructive sleep apnea, and type 2 diabetes.

Treatment-Seeking Status

In accordance with previous studies [11, 12, 26], patients seeking surgery reported significantly lower physical health according to the SF-36. However, patients in many of these studies did not have any appropriate alternative to surgery. In the MOBIL study, by contrast, patients had two different obesity treatment choices: bariatric surgery or an intensive (partly residential) lifestyle program.

Limitations

Our cross-sectional study has limitations. Firstly, the finding of a positive association between work status and HRQoL does not infer any causal relationship. As such, there is a need for further exploration through longitudinal studies. Secondly, the "healthy worker effect," a phenomenon of any group of workers likely to be more healthy than the population as a whole, can give rise to both selection and confounding bias [27]. Occupational groups of patients often have fewer illnesses and disabilities and as such are more likely to be healthy than the patient population as a whole. Thirdly, it may be hypothesized that various levels of disability partly explain both poor HRQoL and unemployment. Unfortunately, since the precise level of disability was not assessed in the present study, we could not test this hypothesis. Finally, our results may not be valid in non-white populations.

Conclusions

In summary, our study of predominantly white morbidly obese subjects has shown that being employed was significantly associated with better general physical and

mental HRQoL and that female gender was significantly associated with the negative emotional results of obesity.

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Paper II

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HEALTH AND QUALITY OF LIFE OUTCOMES

RESEARCH Open Access

Health related quality of life after gastric bypass or intensive lifestyle intervention: a controlled clinical study

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Abstract

Background: There is little robust evidence relating to changes in health related quality of life (HRQL) in morbidly obese patients following a multidisciplinary non-surgical weight loss program or laparoscopic Roux-en-Y Gastric Bypass (RYGB). The aim of the present study was to describe and compare changes in five dimensions of HRQL in morbidly obese subjects. In addition, we wanted to assess the clinical relevance of the changes in HRQL between and within these two groups after one year. We hypothesized that RYGB would be associated with larger improvements in HRQL than a part residential intensive lifestyle-intervention program (ILI) with morbidly obese subjects.

Methods: A total of 139 morbidly obese patients chose treatment with RYGB (n=76) or ILI (n=63). The ILI comprised four stays (seven weeks) at a specialized rehabilitation center over one year. The daily schedule was divided between physical activity, psychosocially-oriented interventions, and motivational approaches. No special diet or weight-loss drugs were prescribed. The participants completed three HRQL-questionnaires before treatment and 1 year thereafter. Both linear regression and ANCOVA were used to analyze differences between weight loss and treatment for five dimensions of HRQL (physical, mental, emotional, symptoms and symptom distress) controlling for baseline HRQL, age, age of onset of obesity, BMI, and physical activity. Clinical relevance was assessed by effect size (ES) where ES<.49 was considered small, between .50-.79 as moderate, and ES>.80 as large.

Results: The adjusted between group mean difference (95% CI) was 8.6 (4.6,12.6) points (ES=.83) for the *physical dimension*, 5.4 (1.5–9.3) points (ES=.50) for the *mental dimension,* 25.2 (15.0–35.4) points (ES=1.06) for the *emotional dimension,* 8.7 (1.8–15.4) points (ES=.37) for the measured *symptom distress,* and 2.5 for (.6,4.5) fewer *symptoms (ES=.56)*, all in favor of RYGB. Within-group changes in HRQOL in the RYGB group were large for all dimensions of HRQL. Within the ILI group, changes in the emotional dimension, symptom reduction and symptom distress were moderate. Linear regression analyses of weight loss on HRQL change showed a standardized beta-coefficient of –.430 (p<.001) on the physical dimension, –.288 (p=.004) on the mental dimension, –.432 (p<.001) on the emotional dimension, .287 (p=.008) on number of symptoms, and .274 (p=.009) on reduction of symptom pressure.

Conclusions: Morbidly obese participants undergoing RYGB and ILI had improved HRQL after 1 year. The weaker response of ILI on HRQL, compared to RYGB, may be explained by the difference in weight loss following the two treatments.

Trial registration: Clinical Trials.gov number NCT00273104

Keywords: Quality of life, Bariatric surgery, Lifestyle modification

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Introduction

Morbid obesity is understood as a body mass index (BMI) ≥40 kg/m^2 or BMI ≥35 kg/m^2 with comorbidities [1]. Roux-en-Y Gastric Bypass (RYGB) is an effective and commonly used [2] surgical procedure for treatment of morbid obesity. Although the majority of patients may prefer non-surgical intervention, bariatric surgery has been shown to be more effective than lifestyle intervention at improving weight loss and obesity associated morbidities [3,4].

Improving patients' health-related quality of life (HRQL) is an important treatment goal. This concept refers to how well an individual functions in daily life and their perceived well-being [5]. In accordance with the World Health Organization's multidimensional definition of health [6], we conceptualize HRQL as encompassing physical, mental and emotional dimensions as well as the burden of obesity specific symptoms.

Few studies have addressed the comparative effects of bariatric surgery and lifestyle intervention on HRQL. The Swedish Obese Subjects research program (SOS), a 10-year non-randomized controlled longitudinal study, compared patients undergoing various bariatric procedures (n=655) with patients (n=621) undergoing conventional weight-loss treatment [7]. Notably, treatment for the conventionally treated patients was not standardized and treatment regimens varied according to local practices. The Swedish study showed that patients who chose surgery lost about 15 times more weight than non-surgically treated patients, mean (SD) loss of 19.7 (15.8) kg vs. 1.3 (13.8) kg. In addition, the study reported that the surgical groups sustained positive outcomes in HRQL compared to non-surgical matched controls. This effect was mainly explained by weight loss. A two-year controlled non-randomized study by Kolotkin et al. [8] found significant improvements in HRQL in patients undergoing RYGB (n=308) compared to a control group of patients who sought but did not undergo RYGB (n=253) and a population-based group of obese individuals (n=272).

Notably, neither study predefined the lifestyle intervention for the non-surgical groups making comparison between bariatric surgery and comprehensive lifestyle programs difficult. The evidence thus remains limited regarding HRQL following RYGB in comparison to specific comprehensive and multidisciplinary lifestyle interventions. In addition, most studies of HRQL in morbid obesity have focused on the physical and mental aspects, applying generic instruments of HRQL measurement. However, the development of obesity-specific HRQL instruments enables additional analyses of the emotional and symptomatic dimensions. Furthermore, only a few studies of HRQL in the morbidly obese have calculated the effect size (ES) of change in HRQL, which underscores the clinical relevance of the various treatments.

An earlier report [9] demonstrated that type 2 diabetes and obesity-related cardiovascular risk factors such as hypertension and hyperlipidemia were improved after both RYGB and a pre-defined part residential multidisciplinary non-surgical intensive lifestyle-intervention program (ILI). However, the improvements were greatest in those patients treated with RYGB. This study did not evaluate the individuals' subjective notion of well-being or how their daily life functioned following these two interventions.

The aim of the present study was to describe and compare changes in five dimensions of HRQL (physical, mental, emotional, number of symptoms, and symptom distress) following RYGB and ILI in morbidly obese subjects. Secondarily, we wanted to assess the clinical relevance of the changes in HRQL between and within these two groups after one year. We hypothesized that RYGB would be associated with larger improvements of HRQL than ILI in morbidly obese subjects.

Methods and procedures

This is a preplanned analysis of data from the MOBIL-study (Morbid Obesity treatment, Bariatric surgery versus Intensive Lifestyle intervention, Clinical Trials.gov number NCT00273104), a non-randomized controlled study designed to compare the effects of bariatric surgery and intensive lifestyle intervention on various comorbidities, eating behavior and HRQL.

A total of 228 patients were screened, with 47 found not to be eligible. Of the remaining 181 participants 35 were not enrolled, leaving 146 in the study (Figure 1, flow of participants).

During the screening procedure all eligible patients underwent a thorough assessment at the Morbid Obesity Center by a multidisciplinary team consisting of an internist, a dietician, a physiotherapist and a trained "obesity" nurse. Patients were provided information about the possible risks and benefits of an operation and also encouraged to incorporate their own values and preferences into the decision-making process. If no contraindication against surgery existed, the patient and the physician together agreed upon the most appropriate choice of therapy; either surgical or conservative [10].

A previous report [9] showed a mean (SD) 1-year weight loss of 30 (8)% of initial body weight in the RYGB group and 8 (9)% in the ILI group. This corresponds to a mean (SD) loss of excess weight above 25 kg/m^2 of 67% (18) and 20% (23) (P<0.001) respectively. The patients in the RYGB group lost a mean (SD) of 14.0 (4.1) BMI points and the ILI group 3.7 (4.2) BMI points. The number of subjects in the RYGB group and ILI group who either moved from being inactive to active (12 vs 18), stayed inactive or active (57 vs 32), or moved from being active to inactive (4 vs 5), differed significantly between the groups. Overall, there was a greater

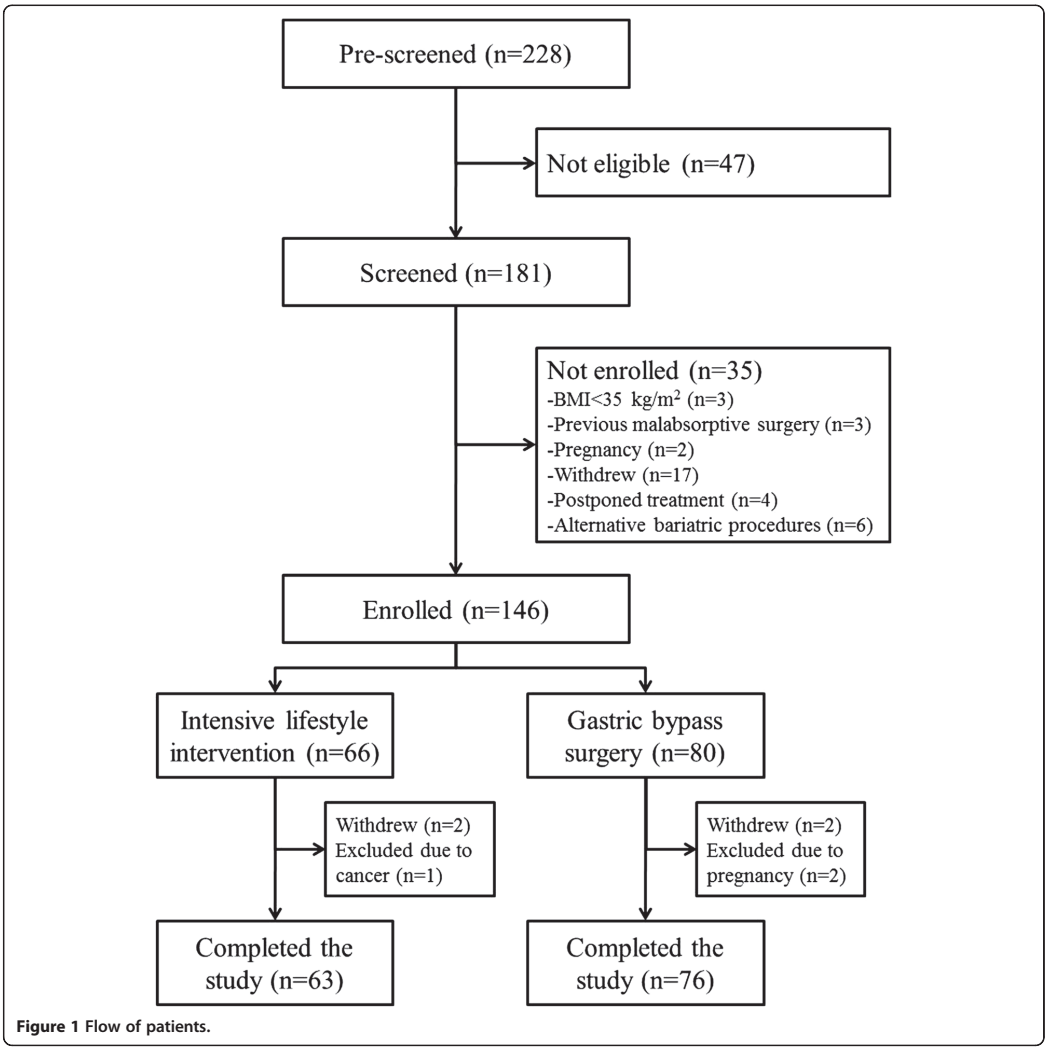

Figure 1 Flow of patients.

increase in the physical activity level of the lifestyle group compared to the surgery group.

The Norwegian Regional Ethics Committee for Medical Research approved the study protocol (S-05175), and the study was performed in accordance with the Declaration of Helsinki. All participants gave informed written consent before enrolment.

Variables, measurement and outcomes

The main outcome in the current analysis was the change in each of the five dimensions of HRQL, conceptualized as encompassing physical, mental and emotional dimensions, as well as the number and burden of obesity-specific symptoms. Since we aimed to compare the effect of two treatment methods, and since entering both weight loss and type of treatment into the same statistical analysis led to multicollinearity (r=.81), weight loss was excluded from the multiple regression analyses of covariance (ANCOVA). Variables that were considered possible confounders included age and BMI prior to intervention, age at the onset of obesity, physical activity and HRQL-score prior to intervention. Three questionnaires were used to measure HRQL: the Medical Outcome Study 36 – Item Short Form Health

Survey (SF-36), the Obesity and Weight-Loss Quality of Life (OWLQOL), and the Weight Related Symptom Measure (WRSM).

Medical Outcome Study 36 – Item Short Form Health Survey (SF-36)

SF-36 is a commonly used generic measure of HRQL based on 36 questions or items [11-13]. Item 2 is not included in the scoring of the instrument [13]. The remaining 35 items form eight subscales (physical function, role physical, bodily pain, general health, role emotional, social function, vitality, and mental health) which can be combined into two summary scores; the physical and mental dimensions [14]. As the validity of the subscales in morbidly obese patients is uncertain [15,16] we studied the physical and mental dimensions. The calculations were performed as recommended by the scale authors [14], using Norwegian norms [17] and oblique factor scores to account for the correlation between the two HRQL-dimensions. The scores were calculated by multiplying each subject's SF-36 subscale z score by its respective factor coefficient and then standardizing each to a T score with a mean of 50 and a standard deviation of 10 [14]. Both scales were set to a range from 0–100, where higher scores indicate better HRQL.

Obesity and Weight-Loss Quality of Life (OWLQOL)

The OWLQOL [18,19] primarily measures emotions and feelings [20,21] which are believed to result from being obese and trying to lose weight. The instrument consists of 17 statements about weight-related feelings and emotions which are rated on a seven-point scale that ranges from 0 ("not at all") to 6 ("a very great deal"). The 17 items of the OWLQOL form a scale ranging from 0–102, with higher scores indicating greater emotional HRQL.

Weight Related Symptom Measure (WRSM)

The WRSM [18,19] measures 20 obesity-specific symptoms using two different sets of items. The first set assesses whether or not the patient is experiencing specific symptoms. The scoring of this set of items creates an additive scale summing up the number of symptoms, ranging from 0–20. The second set of items concerns the distress of the symptoms, with values from 0 ("not at all") to 6 ("bothers a very great deal"). They form a symptom distress scale ranging from 0–120, where higher scores indicate greater symptom distress. Both the OWLQOL and the WRSM were obtained with permission from the Seattle Quality of Life Group, University of Washington.

In sum, the three HRQL questionnaires constitute five different measurements of HRQL; physical dimension (SF-36), mental dimension (SF-36), emotional dimension (OWLQOL), number of obesity symptoms (WRSM), and distress of obesity symptoms (WRSM).

Changes in scores between two time-points or groups can be statistically significant. An important follow-up question is whether the changes are clinically relevant. There are different approaches to addressing this. Here we have chosen the effect size (ES) to grade the efficiency of surgical versus nonsurgical treatment [22,23].

Physical activity was assessed through structured interviews performed by registered dieticians. Time spent performing light (e.g. casual walking), moderate (e.g. brisk walking) and vigorous (e.g. jogging) intensity aerobic physical activities for periods of 10 minutes or more was recorded. Participants who performed 150 minutes or more per week of moderately intense aerobic physical activities were considered to be physically active, as were those participants who performed 60 minutes or more per week of vigorously intense aerobic physical activities [24].

Participants

A total of 139 patients completed the MOBIL-study (Figure 1). At baseline, all patients in both the RYGB group (n=76) and the ILI group (n=63) completed the three HRQL instruments. At 1 year follow up 62 (82%) participants in the RYGB group and 48 (76%) in the ILI group had completed the questionnaires. In order to assess the representativeness of the sample at the end of the study we used an independent samples *t*-test to compare differences between patients not completing the questionnaires at the end of the study versus completers. Patients who did not complete the questionnaires after 1 year (n=29) were comparable with those who did (n=110) with regards to baseline HRQL, gender, age, body weight, employment status, and weight loss after 1 year (data not shown).

Interventions

During follow-up, patients allocated to RYGB were examined by a bariatric surgeon 6 weeks after surgery, while patients were seen by a dietician quarterly, usually in groups of 12–16. The patients in the ILI group were admitted to a rehabilitation center specializing in the care of morbidly obese patients. The aim was to attain a sustained 1-year weight loss ≥10%. Each patient was encouraged to increase their physical activity and to normalize eating habits. The program intended to increase each patient's self-efficacy in dealing with their weight problem, as well as an improvement in self-esteem.

The 1-year lifestyle program comprised four stays at the rehabilitation center – three 5-day stays in weeks 1, 26, and 51, and a four-week stay from weeks 13–17 (Figure 2).

The daily schedule was divided between organized daily physical activity (3–4 hours) and various psychosocially-oriented interventions combined with a motivational approach both in group sessions and individual sessions (3–4 hours). These sessions were supervised by a medical doctor, nutritionists, physiotherapists and mental health-trained nurses. No special diet or weight-loss drugs were prescribed, but patients were encouraged to follow the guidelines of the Norwegian National Council of Nutrition [25], which recommends that the daily intake of protein, fat, carbohydrate and alcohol should account respectively for 10–20, <30, 50–60, and <5% of energy consumed. In addition, the patients were asked to reduce their daily total energy intake, but not using calorie-counting. Outside of these stays patients were contacted by phone once every 2 weeks. They were also encouraged to self-monitor their eating habits and physical activities in a pre-fabricated diary, as well as to consult their general practitioner for weight measurement and follow-up every four weeks.

Statistical methods

Data are presented as mean (SD) or n (%) unless otherwise stated. Skewed data were transformed to approximate normality using natural logarithms. To assess the reliability of the HRQL-scales we calculated Cronbach's alpha coefficients.

After applying Little's test of randomness of missing data, missing values (SF-36:23.5%, OWLQOL:24.5%, WRSM:23.7%) were imputed using multiple imputation. The imputation model consisted of the HRQL-scores, physical activity at baseline and 1 year, and age of onset of obesity as predictor and imputation variables, and treatment, gender, age, baseline BMI, marital status, employment, and education as predictor variables. Through a fully conditional specification model, applying linear regression as the prediction method for scale variables and two-way interactions for categorical variables, we generated twenty complete datasets for each of the HRQL-scores with 10 iterations per dataset. The statistical analyses were performed on each complete dataset, and thereafter the multiple analyses results were combined to achieve single estimates. The combined estimates are presented. Observing the fraction of missing information, relative increase variance, and relative efficiency, the imputed data-sets (n=139) were comparable with the original data-set (n=110) in terms of the imputed variables (data not shown).

Within-group analyses in both groups were performed using paired samples *t*-test. Between-group comparisons at baseline were analyzed using independent samples *t*-test for continuous variables and χ^2 for categorical variables.

Within groups ES was calculated as the mean HRQL change score between 1 year and baseline divided by the standard deviation of the baseline HRQL. Between groups ES was calculated as the difference in mean HRQL change score between groups at 1 year divided by the standard deviation of baseline HRQL [22,23]. An ES from .20–.49 was considered small, .50–.79 as moderate, and greater than .80 as large [22,23].

In order to avoid problems of regression towards the mean [26,27], we applied one-way between-group analyses of covariance (ANCOVA) to compare the effect of RYGB and lifestyle intervention on five dimensions of HRQL. Age at baseline, age at the onset of obesity, BMI at baseline, physical activity at baseline, and baseline HRQL-scores were used as covariates in each of the five analyses [28]. Assessments of normality, linearity, homogeneity of variance and regression slopes were conducted to ensure assumptions for the ANCOVA. The unadjusted changes from baseline in the RYGB group and ILI group, together with the adjusted between group differences (95% CI), are reported. To account for the percentage explained variance in the dependents, calculations of partial eta squared (ηp^2) were performed. To test the effect of weight reduction (instead of treatment choice) on HRQL, multiple linear regression analyses were conducted with each of the 12 months HRQL changes (physical, mental, emotional, number of obesity symptoms, and symptom distress) as dependents, with gender, age at baseline, age at the onset of obesity, BMI at baseline, physical activity at baseline, and weight change in per cent of baseline weight as independents. Throughout, we report two-tailed P values, with P<.05 was considered to be statistically significant. The statistical analysis was conducted using SPSS v.18.0.

Results

Internal consistency

The inter-item analyses showed Cronbach's alpha coefficients >.80, indicating that intercorrelations among the items is high and that there is a high reliability for all of the HRQL-scales (physical, mental, and emotional dimensions, number of symptoms, and symptom distress).

Figure 2 Schedule of stays during the 1-year intensive lifestyle intervention program at the rehabilitation centre.

Patients

Baseline demographic characteristics are summarized in Table 1. Compared to the ILI group, the patients in the RYGB group had a higher BMI (ES=.49), were younger (ES=.36), had earlier onset of obesity (ES=.47), and had lower physical (ES=.50) and emotional HRQL (ES=.42).

Changes in the five main dimensions of HRQOL

Adjusted between group analyses, controlling for the effects of treatment, age at baseline, age at the onset of obesity, BMI at baseline, physical activity at baseline, and baseline HRQL-scores, showed that compared to the ILI group, the RYGB group had statistically significant higher adjusted mean improvement in all HRQL-measurements, especially the emotional dimension (Table 2). Based on calculations of ηp^2, type of treatment predicted 19.7% of the variance (ES=.83) in the physical dimension change score, 9.8% (ES=.50) in the mental dimension change score, 22.6% (ES=1.06) in the emotional dimension change score, 7.7% (ES=.56) in the number of symptoms, and 8.1% (ES=.37) in the symptom distress change score.

Unadjusted within-group analyses showed that both groups reported improvements in all five HRQL-measurements (Figures 3 and 4). All effect sizes were large within the RYGB group and small to moderate within the ILI group.

Table 1 Demographic, socioeconomic and clinical characteristics of 139 morbidly obese individuals who chose a part residential intensive lifestyle intervention program (ILI) or gastric bypass surgery (RYGB)

Variable	Total (n=139)	RYGB (n=76)	ILI (n=63)	P-value
Women (n, %)	97 (70%)	53 (70%)	44 (70%)	.569
Age (years), mean (SD)	46 (11)	43 (11)	47 (11)	.021
Onset of obesity (n, %)				
<12 years	35 (25%)	25 (33%)	10 (16%)	
12-20 years	28 (20%)	17 (22%)	11 (17%)	
>20 years	76 (55%)	34 (45%)	42 (67%)	.003
BMI (kg/m^2), mean (SD)	44 (6)	46 (6)	43 (5)	<.001
Married/cohabitant, (n, %)	83 (60%)	45 (60%)	38 (60%)	.895
Employment (n, %)	82 (59%)	40 (53%)	42 (67%)	.094
Length of education (n, %)				
Basic (<9 year)	32 (23%)	18 (24%)	14 (22%)	
Intermediate (9–12 year)	75 (54%)	44 (58%)	31 (49%)	
Higher (>12 year)	2 (23%)	14 (18%)	18 (29%)	.358
Physical activity (n, %)				
Low	115 (83%)	67 (88%)	48 (76%)	
High	24 (17%)	9 (12%)	15 (24%)	.063
Quality of life scores, mean (SD)				
Physical dimension [a]	36 (10)	34 (10)	39 (10)	.018
Mental dimension [a]	41 (11)	41 (11)	42 (11)	.690
Emotional dimension [b]	36 (24)	32 (23)	42 (24)	.047
Number of symptoms [c]	11 (4)	12 (4)	11 (4)	.343
Symptom distress [d]	41 (21)	43 (21)	38 (20)	.173

(a) SF-36 (scale 0–100). (b) OWLQOL (scale 0–102). (c) WRSM (scale 0–20). (d) WRSM (scale 0–120).

Changes in self-reported symptom distress

Twenty common obesity specific health problems associated with obesity are listed in Table 3. Compared to the ILI group, the RYGB group showed greater improvement in ailments such as reduced physical stamina, joint pain, snoring, sleep problems, skin irritation, water retention, and foot problems. Only the improvements of physical stamina and joint pain showed large effect sizes between groups. On the other hand, the RYGB group reported higher sensitivity to cold (Table 3), and this difference was considered large.

The effect of weight reduction

The linear regression analyses revealed significant associations between weight reduction in per cent of baseline weight, when controlling for the effect of gender, age at baseline, age at the onset of obesity, BMI at baseline, and physical activity at baseline. The analyses of weight loss on HRQL change showed a standardized beta-coefficient of −.430 (p<.001) on the physical dimension, −.288 (p=.004) on the mental dimension, −.432 (p<.001) on the emotional dimension, .287 (p=.008) on number of symptoms, and .274 (p=.009) on reduction of symptom pressure.

Discussion

Key results

In this non-randomized clinical trial comparing RYGB to ILI, we found that RYGB was more effective at improving all HRQL-dimension scores (Table 2). In particular, the RYGB group had a clinically relevant effect on changes in the emotional dimension (ES=1.06) and in the physical dimension (ES=.83). Within the RYGB group all HRQL dimensions showed large improvements (ES>.80). Within the ILI group, changes were moderate (ES>.50 and <.79).

Previous studies have shown that patients treated with RYGB experience larger improvements of HRQL compared to those undergoing conventional weight loss treatment [7,8]. However, these studies did not compare the surgical procedures with a part residential lifestyle intervention program. In addition, the authors did not assess the effect sizes of the treatments on the various dimensions of HRQL.

The improvement of the emotional dimension of HRQL was particularly pronounced in the RYGB group.

Table 2 One way between-groups analysis of variance on five dimensions of HRQL in morbidly obese patients undergoing either RYGB or ILI

	Changes from baseline		Adjusted between group difference, mean (95% CI)	P	ES
	RYGB (n=76)	ILI (n=63)			
Physical dimension[a]	16.8 (9.7)	4.9 (9.4)	8.6 (4.6,12.6)	<.001	.83
Mental dimension[a]	9.6 (9.1)	3.5 (8.9)	5.4 (1.5,9.3)	.007	.50
Emotional dimension[b]	42.7 (25.5)	15.7 (21.7)	25.2 (15.0,35.4)	<.001	1.06
Number of obesity symptoms[c]	−5.3 (4.6)	−2.9 (4.7)	−2.3 (−4.5,-.6)	.012	.56
Symptom distress[d]	−25.2 (20.7)	−14.3 (16.5)	−8.7 (−15.4,-1.8)	.013	.37

Adjustments were made for age at the onset of obesity and baseline values of age, BMI physical activity level, and HRQL. (a) SF-36 (scale 0–100). (b) OWLQOL (scale 0–102). (c) WRSM (scale 0–20). (d) WRSM (scale 0–120). Statistical significance (P) and effect size (ES) are reported.

A possible explanation may be that the massive weight loss following RYGB after 1 year reduced the patients feeling of being fat and, accordingly, improved their feeling of being "normal". The surgical procedure per se seems to help many patients gain control over their food intake, thus confirming the clinical observation of more "relaxed" patients one year after surgery. In addition, as suggested by Fabricatore and Wadden [29], the negative stigma associated with obesity may be caused by an undesirable body appearance and by the "character defects" other people associate with this appearance. In our terms, as patients start to experience massive weight loss, their perception of their own body is expected to improve, as is the perceptions of other people. This internal and external reduction of stigma may be followed by an improvement in self-esteem and positive emotions among obese patients experiencing massive weight loss. However, a massive weight loss and a less stigmatizable body appearance may not be the only explanations as to the improvements in the emotional HRQL. The ILI group also reported significant improvements in the emotional dimension of HRQL after 1 year, even though the effect size was moderate. The moderate effect in the ILI group may be explained by the more moderate weight loss in this group. However, weight loss may not be the only explanation. It is conceivable that the intervention itself added to the improvement of emotional HRQL in the ILI group. The group-based focus and motivational approach in the lifestyle program aimed at increasing self-efficacy, self-esteem and mood state. Previous studies seem to support this notion. Programs focusing on motivationally-oriented group sessions report as little as 3 kg. weight loss (e.g. from 103 to 100 kg.) but have found significant improvements in mood state as measured with validated psychometric instruments [30]. In another study of 440 obese patients with

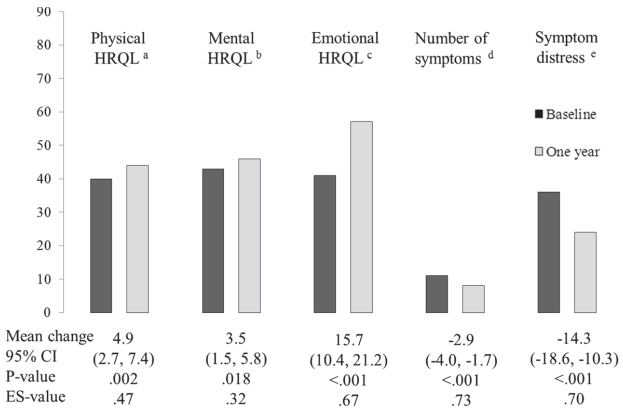

Figure 3 Mean scores on five HRQL-scales at baseline and 1 year in morbidly obese patients who underwent a part residential intensive lifestyle intervention program (n=63). (**a**) SF-36 Physical dimension (0–100). (**b**) SF-36 Mental dimension (0–100). (**c**) OWLQOL Emotional dimension (0–102). (**d**) WRSM symptom number score (0–20). (**e**) WRSM symptom severity score (0–120). Unadjusted mean change scores and 95% CI. P and ES-values for within-group changes.

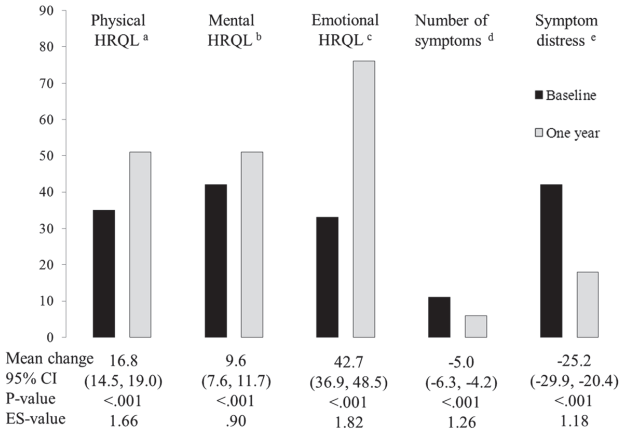

Figure 4 Mean scores on five HRQL-scales at baseline and 1 year in morbidly obese patients who underwent RYGB (n=76). (**a**) SF-36 Physical dimension (0–100). (**b**) SF-36 Mental dimension (0–100). (**c**) OWLQOL Emotional dimension (0–102). (**d**) WRSM symptom number score (0–20). (**e**) WRSM symptom distress score (0–120). Unadjusted mean change scores and 95% CI. P and ES-values for within-group changes.

Table 3 1-year changes in reported symptom distress between groups of morbidly obese patients undergoing RYGB (n=76) or intensive lifestyle intervention (n=63)

Symptom	RYGB	ILI	P	ES
Physical stamina	−2.7 (2.5)	-.7 (2.6)	<.001	.913
Pain in the joints	−2.4 (2.2)	-.7 (2.0)	.002	.891
Snoring	−2.3 (2.2)	-. 8 (2.0)	.002	.721
Sensitivity to cold	1.4 (2.2)	.1 (1.9)	.005	.921
Skin irritation	−1.2 (1.9)	-.3 (1.8)	.032	.493
Sleep problems	−1.3 (2.2)	-.4 (2.2)	.043	.406
Water retention	−1.5 (1.9)	-.6 (2.0)	.047	.456
Foot problems	−2.2 (2.6)	−1.1 (2.5)	.050	.541
Back pain	−1.6 (2.0)	-.9 (1.7)	.071	.350
Tiredness	−1.6 (2.2)	-.7 (2.2)	.089	.460
Shortness of breath	−2.2 (2.1)	−1.4 (1.9)	.093	.442
Leakage of urine	-.8 (1.6)	-.3 (2.0)	.220	.267
Frequent urination	-.8 (2.1)	-.3 (1.7)	.281	.244
Increased sweating	−1.3 (2.1)	-.9 (2.2)	.339	.246
Loss of sexual desire	−1.4 (2.6)	-.9 (2.6)	.393	.215
Lightheadedness	.3 (1.8)	-.2 (1.5)	.517	.164
Increased thirst	-.9 (1.9)	-.7 (1.8)	.569	.136
Increased irritability	-.4 (2.1)	-.7 (2.1)	.595	.140
Increased appetite	-.2 (2.2)	-.3 (2.0)	.849	.044
Sensitivity to heat	−1.5 (2.4)	−1.6 (2.2)	.987	.004

Self-reported data from the Weight-related Symptom Measure (WRSM). Scale from 0 (bothers not at all) to 6 (bothers a very great deal). Data are given as given as mean difference in scores (SD). P and ES-values for between-group differences.

coronary artery disease, group support was reported to be associated with a significant improvement in the mental dimension of HRQL despite moderate weight loss [31].

The self-reported symptom scores before treatment in both groups corroborate the well-known association between high BMI, several comorbidities and physical HRQL. After 1 year we found that patients in both groups reported significantly fewer symptoms. The improvements in joint pain and physical stamina in the RYGB group were notable and may, together with improvements in skin irritation, water retention, foot problems, and shortness of breath, have resulted in easier performance of everyday personal hygiene, housekeeping, shopping and walking. All these tasks are central elements of the physical dimension of HRQL [11], which in the RYGB group showed a large effect size (ES=.83).

Another distressing obesity-associated symptom is snoring and tiredness. These symptoms were markedly reduced in the RYGB group. This finding supports a report from the SOS-study which found a substantial reduction in symptoms of sleep apnoea and daytime sleepiness in the bariatric surgery group after 2 years [32]. One might speculate that increased sleep quality and reduced daytime sleepiness may lead to increased vitality and improved functioning at work or during other daily activities, which also is embedded in the physical dimension of HRQL [11]. The finding of increased sensitivity to cold in the RYBG group is probably connected to the higher loss of fat mass with surgery [33], and

is a phenomenon commonly observed within clinical practice.

The overall reduction of the number of symptoms and symptom distress in the ILI group was statistically significant, although with moderate effect sizes. However, compared to the RYGB group more patients in the ILI group were physically active at baseline, whilst the increase in physical activity after one year was larger in the ILI group than the RYGB group [9]. We believe that the combination of the overall reduction in symptom distress and higher activity levels contributed to an improvement of the physical HRQL in the ILI group, even though the weight loss was moderate. There is a consistent association of higher HRQL scores with higher levels of physical activity among healthy adults in cross-sectional studies [34], and this association is stronger on the physical dimension of the HRQL than the mental dimension [34]. We also know that interventions combining physical activity and diet improve the physical dimension of HRQL but not the mental dimension among older obese individuals with knee ostoearthritis [35].

As with the emotional and physical aspects of HRQL, the mental aspects also improved in both groups after 1 year. The RYGB group scored significantly better than the ILI group. Other studies have found similar results [7,8] between bariatric surgery and non-standardised lifestyle programs. However, our study extends previous findings to include the comparative effects of a structured, systematic part residential lifestyle program. The improvements in the mental dimension of HRQL may be explained by the greater weight loss and improvement of psychosocial status including social relations and employment opportunities [36]. A deeper understanding of the relationship between weight loss and improvement of the emotional and mental dimension of HRQL may necessitate research designs other than a quantitative approach.

We have previously shown [9] bariatric surgery to be superior to lifestyle treatment in regards to weight loss. However, the effect of weight loss on improvement of HRQL may have been moderated by the lifestyle treatment regime itself. In particular, our results suggest that a "comprehensive and multidisciplinary program intended to increase the patient's self-efficacy in dealing with their weight problem" may impact upon HRQL, independent of weight loss.

As reported earlier our study has limitations [9]. Although preferable when conducting a clinical trial, we did not find randomization to be appropriate. According to Norwegian guidelines, treatment seeking morbidly obese subjects should be offered either conservative or surgical therapy. We therefore considered it unethical to assign patients to surgery if they qualified for a lifestyle intervention program and preferred this course of treatment to surgery. This stance also held vice versa. Thus, the differences between the groups may not be causally associated with choice of treatment. Further, the study was limited to a 1-year time span. The long term effects of the two interventions on HRQOL may differ due to intervening life events, complications of surgery, or other reasons, and these require further study.

Lifestyle intervention for morbid obesity comprises of many different methods, from very low calorie diets to comprehensive psychosocially oriented programs combining diets, physical activity and behavioral intervention. There is little robust evidence identifying the most effective lifestyle strategies for treatment and prevention of obesity in general and in morbid obesity in particular [37]. Hence, research must focus on a variety of lifestyle intervention programs in order to to identify the most beneficial treatment regimens. Our findings indicate that a pre-defined part residential multidisciplinary non-surgical weight loss program with a psychosocially-oriented motivational approach is a promising intervention when aiming to increase HRQL in morbidly obese patients. However, larger weight losses may be necessary to maximize the beneficial effects.

Conclusion

Our study shows that following a part residential multidisciplinary lifestyle intervention program, morbidly obese patients improved their HRQL, although patients undergoing bariatric surgery experienced larger improvements in HRQL after 1 year. The higher clinical relevance of bariatric surgery on HRQL may be explained by a higher weight loss.

Competing interests

Tor-Ivar Karlsen is a PhD-fellow at the Morbid Obesity Centre and works at the University of Agder. He is supported financially through an unrestricted educational grant from Evjeklinikken AS. All the other authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

Authors' contributions

TIK participated in the design of the study, collected data from patients, analyzed the data and drafted the manuscript. RSL, ST, GKN revised and helped draft the manuscript, JR revised and helped draft the manuscript and assessed the statistical analyses, RS and JH designed the study and revised and helped draft the manuscript. All authors read and approved the final manuscript.

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Paper III

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Appendix 1 SF-36

Dato:.....

SF-36 SPØRRESKJEMA OM HELSE

INSTRUKSJON: Dette spørreskjemaet handler om hvordan du ser på din egen helse. Disse opplysningene vil hjelpe oss til å få vite hvordan du har det og hvordan du er i stand til å utføre dine daglige gjøremål.

Hvert spørsmål skal besvares ved å sette en ring rundt det tallet som passer best for deg. Hvis du er usikker på hva du skal svare, vennligst svar så godt du kan.

1. Stort sett, vil du si at din helse er: (sett ring rundt et tall)

Utmerket.....	1
Meget god	2
God.....	3
Nokså god.....	4
Dårlig.....	5

2. Sammenlignet med for ett år siden, hvordan vil du si at din helse stort sett er nå?

(sett ring rundt et tall)

Mye bedre nå enn for ett år siden.....	1
Litt bedre nå enn for ett år siden	2
Omtrent det samme som for ett år siden.....	3
Litt dårligere enn for ett år siden.....	4
Mye dårligere nå enn for ett år siden.....	5

3. De neste spørsmålene handler om aktiviteter som du kanskje utfører i løpet av en vanlig dag. Er din helse slik at den begrenser deg i utførelsen av disse aktivitetene nå? Hvis ja, hvor mye?

(sett ring rundt et tall på hver linje)

AKTIVITETER	**Ja, begrenser meg mye**	**Ja, begrenser meg litt**	**Nei, begrenser meg ikke i det hele tatt**
a. Anstrengede aktiviteter som å løpe, løfte tunge gjenstander, delta i anstrengende idrett	1	2	3
b. Moderate aktiviteter som å flytte et bord, støvsuge, gå en tur eller drive med hagearbeid	1	2	3
c. Løfte eller bære en handlekurv	1	2	3
d. Gå opp trappen flere etasjer	1	2	3
e. Gå opp trappen en etasje	1	2	3
f. Bøye deg eller sitte på huk	1	2	3
g. Gå mer enn to kilometer	1	2	3
h. Gå noen hundre meter	1	2	3
i. Gå hundre meter	1	2	3
j. Vaske deg eller kle på deg	1	2	3

4. I løpet av de siste 4 ukene, har du hatt noen av de følgende problemer i ditt arbeid eller i andre av dine daglige gjøremål på grunn av din fysiske helse?

(sett ring rundt et tall på hver linje)

	JA	**NEI**
a. Du har måttet **redusere tiden** du har brukt på arbeid eller på andre gjøremål	1	2
b. Du har **utrettet mindre** enn du hadde ønsket	1	2
c. Du har vært hindret i å utføre **visse typer** arbeid eller gjøremål	1	2
d. Du har hatt **problemer** med å gjennomføre arbeidet eller andre gjøremål (f.eks fordi det krevde ekstra anstrengelser)	1	2

5. I løpet av de siste 4 ukene, har du hatt noen av de følgende problemer i ditt arbeid eller i andre av dine daglige gjøremål på grunn av følelsesmessige problemer (som f.eks. å være deprimert eller engstelig)

(sett ring rundt et tall på hver linje)

	JA	NEI
Du har måttet **redusere tiden** du har brukt på arbeid eller på andre gjøremål	1	2
Du har **utrette mindre** enn du hadde ønsket	1	2
Du har utført arbeidet eller andre gjøremål mindre **grundig** enn vanlig	1	2

6. I løpet av de siste 4 ukene, i hvilken grad har din fysiske helse eller følelsesmessige problemer hatt innvirkning på din vanlige sosiale omgang med familie, venner, naboer eller foreninger?

(sett ring rundt ett tall)

Ikke i det hele tatt..... 1

Litt..... 2

Endel..... 3

Mye..... 4

Svært mye..... 5

7. Hvor sterke kroppslige smerter har du hatt i løpet av de siste 4 ukene?

(sett ring rundt ett tall)

Ingen..... 1

Meget svake..... 2

Svake..... 3

Moderate..... 4

Sterke..... 5

Meget sterke..... 6

8. I løpet av de siste 4 ukene, hvor mye har smerter påvirket ditt vanlige arbeid (gjelder både arbeid utenfor hjemmet og husarbeid)?

(sett ring rundt ett tall)

Ikke i det hele tatt.....	1
Litt.....	2
Endel.....	3
Mye.....	4
Svært mye.....	5

9. De neste spørsmålene handler om hvordan du har følt deg og hvordan du har hatt det de siste 4 ukene. For hvert spørsmål, vennligst velg det svaralternativet som best beskriver hvordan du har hatt det. Hvor ofte i løpet av de siste 4 ukene har du:

(sett ring rundt ett tall på hver linje)

	Hele Tiden	**Nesten hele tiden**	**Mye av tiden**	**Endel av tiden**	**Litt av tiden**	**Ikke i det hele tatt**
a. Følt deg full av tiltakslyst?	1	2	3	4	5	6
b. Følt deg veldig nervøs?	1	2	3	4	5	6
c. Vært så langt nede at ingenting har kunnet muntre deg opp?	1	2	3	4	5	6
d. Følt deg rolig og harmonisk?	1	2	3	4	5	6
e. Hatt mye overskudd?	1	2	3	4	5	6
f. Følt deg nedfor og trist?	1	2	3	4	5	6
g. Følt deg sliten?	1	2	3	4	5	6
h. Følt deg glad?	1	2	3	4	5	6
i. Følt deg trett?	1	2	3	4	5	6

Løpenr.:.....

10. I løpet av de siste 4 ukene, hvor mye av tiden har din fysiske helse eller følelsesmessige problemer påvirket din sosiale omgang (som det å besøke venner, slektninger osv.)?

(sett ring rundt ett tall)

Hele tiden.....	1
Nesten hele tiden.....	2
En del av tiden	3
Litt av tiden	4
Ikke i det hele tatt.....	5

11. Hvor RIKTIG eller GAL er hver av de følgende påstander for deg?

(sett ring rundt ett tall på hver linje)

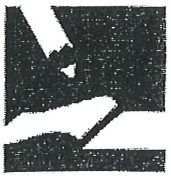
	Helt riktig	**Delvis riktig**	**Vet ikke**	**Delvis gal**	**Helt gal**
a. Det virker som om jeg blir syk litt lettere enn andre	1	2	3	4	5
b. Jeg er like frisk som de fleste jeg kjenner	1	2	3	4	5
c. Jeg tror at helsen min vil forverres	1	2	3	4	5
d. Jeg har utmerket helse	1	2	3	4	5

Appendix 2 OWLQOL

Din helse
-og-
velvære

Spørreskjema om livskvalitet ved overvekt og vektreduksjon (OWLQOL)

Dette spørreskjemaet stiller spørsmål omkring din oppfatning av din egen helse og vekt.



Takk for at du besvarer disse spørsmålene!

Instruksjoner for utfylling av livskvalitets-spørreskjemaet for studiens deltakere

1) Dette spørreskjemaet er en viktig del av den samlede medisinske vurderingen som blir foretatt av deg. Spørsmålene er laget slik at man får samlet informasjon om hvordan du oppfatter at din helse påvirker din livskvalitet.

2) Fyll ut skjemaet med kulepenn. Press hardt og skriv tydelig når du fyller ut skjemaet for å sikre at svarene dine blir lette å lese.

3) Vennligst bruk tid på å lese og besvare hvert spørsmål nøye. Noen spørsmål kan ligne på hverandre, men alle er forskjellige.

4) Vennligst besvar hvert spørsmål ved å sette et ☒ i den rubrikken som best beskriver ditt svar. Du kan endre svar ved å sette en strek (~~☒~~) tvers over alternativet som du ønsker og endre og sette et ☒ i den rubrikken som passer med ditt nye valg.

5) Det er ingen riktige eller gale svar. Hvis du er usikker på hvordan du skal besvare et spørsmål, vennligst gi det beste svaret du kan.

6) Dine svar vil bli behandlet konfidensielt. Studiens koordinator vil kun kontrollere om alle spørsmål er besvart og vil ikke vise dine svar til annet helsepersonale.

Dine følelser om din egen vekt

Nedenfor er det en liste over utsagn om din livskvalitet relatert til det å være overvektig og å forsøke å gå ned i vekt.

Vennligst sett et ☒ i den ene rubrikken som best beskriver ditt svar akkurat nå for hvert av de følgende utsagnene.

	IKKE I DET HELE TATT	NESTEN IKKE	NOE	MODERAT	MYE	TEMMELIG MYE	SVÆRT MYE
1. På grunn av vekten min prøver jeg på å bruke tøy som skjuler fasongen min *(Vennligst kryss av en rubrikk)*	☐0	☐1	☐2	☐3	☐4	☐5	☐6
2. Jeg føler meg frustrert over at jeg har mindre energi på grunn av vekten min *(Vennligst kryss av en rubrikk)*	☐0	☐1	☐2	☐3	☐4	☐5	☐6
3. På grunn av vekten min har jeg skyldfølelse når jeg spiser *(Vennligst kryss av en rubrikk)*	☐0	☐1	☐2	☐3	☐4	☐5	☐6
4. Jeg er plaget av hva andre mennesker sier om vekten min *(Vennligst kryss av en rubrikk)*	☐0	☐1	☐2	☐3	☐4	☐5	☐6
5. På grunn av vekten min forsøker jeg å unngå at det blir tatt bilde av meg *(Vennligst kryss av en rubrikk)*	☐0	☐1	☐2	☐3	☐4	☐5	☐6
6. På grunn av vekten min må jeg være veldig nøye med den personlige hygiene *(Vennligst kryss av en rubrikk)*	☐0	☐1	☐2	☐3	☐4	☐5	☐6
7. Vekten min hindrer meg i å gjøre ting jeg ønsker å gjøre *(Vennligst kryss av en rubrikk)*	☐0	☐1	☐2	☐3	☐4	☐5	☐6
8. Jeg bekymrer meg over den fysiske belastningen som vekten påfører kroppen *(Vennligst kryss av en rubrikk)*	☐0	☐1	☐2	☐3	☐4	☐5	☐6

(Vennligst snu arket)

(fortsatt)...

	IKKE I DET HELE TATT	NESTEN IKKE	NOE	MODERAT	MYE	TEMMELIG MYE	SVÆRT MYE
9. På grunn av vekten min er jeg frustrert over at jeg ikke kan spise det samme som andre *(Vennligst kryss av en rubrikk)*	☐0	☐1	☐2	☐3	☐4	☐5	☐6
10. Jeg føler meg deprimert på grunn av vekten min *(Vennligst kryss av en rubrikk)*	☐0	☐1	☐2	☐3	☐4	☐5	☐6
11. Jeg føler meg stygg på grunn av vekten min (Vennligst kryss av en rubrikk)	☐0	☐1	☐2	☐3	☐4	☐5	☐6
12. Jeg bekymrer meg om fremtiden på grunn av vekten min *(Vennligst kryss av en rubrikk)*	☐0	☐1	☐2	☐3	☐4	☐5	☐6
13. Jeg misunner mennesker som er tynne *(Vennligst kryss av en rubrikk)*	☐0	☐1	☐2	☐3	☐4	☐5	☐6
14. Jeg føler at folk stirrer på meg på grunn av vekten min *(Vennligst kryss av en rubrikk)*	☐0	☐1	☐2	☐3	☐4	☐5	☐6
15. Jeg har vansker med å akseptere kroppen min på grunn av vekten min *(Vennligst kryss av en rubrikk)*	☐0	☐1	☐2	☐3	☐4	☐5	☐6
16. Jeg er bekymret for at jeg vil legge på meg det jeg går ned i vekt *(Vennligst kryss av en rubrikk)*	☐0	☐1	☐2	☐3	☐4	☐5	☐6
17. Jeg blir motløs når jeg forsøker å gå ned i vekt *(Vennligst kryss av en rubrikk)*	☐0	☐1	☐2	☐3	☐4	☐5	☐6

Vennligst gå tilbake til spørsmålene du nettopp har besvart for å forsikre deg om at du ikke har hoppet over noen punkter

Takk for at du besvarte disse spørsmålene!

Appendix 3 WRSM

Din helse
-og-
velvære

Symptommåling ved overvekt (WRSM)

Dette spørreskjemaet stiller spørsmål omkring din oppfatning av din egen helse og vekt.

Takk for at du besvarer disse spørsmålene!

Instruksjoner for utfylling av livskvalitets-spørreskjemaet for studiens deltakere

1) Dette spørreskjemaet er en viktig del av den samlede medisinske vurderingen som blir foretatt av deg. Spørsmålene er laget slik at man får samlet informasjon om hvordan du oppfatter at din helse påvirker din livskvalitet.

2) Fyll ut skjemaet med kulepenn. Press hardt og skriv tydelig når du fyller ut skjemaet for å sikre at svarene dine blir lette å lese.

3) Vennligst bruk tid på å lese og besvare hvert spørsmål nøye. Noen spørsmål kan ligne på hverandre, men alle er forskjellige.

4) Vennligst besvar hvert spørsmål ved å sette et ☒ i den rubrikken som best beskriver ditt svar. Du kan endre svar ved å sette en strek (-☒-) tvers over alternativet som du ønsker og endre og sette et ☒ i den rubrikken som passer med ditt nye valg.

5) Det er ingen riktige eller gale svar. Hvis du er usikker på hvordan du skal besvare et spørsmål, vennligst gi det beste svaret du kan.

6) Dine svar vil bli behandlet konfidensielt. Studiens koordinator vil kun kontrollere om alle spørsmål er besvart og vil ikke vise dine svar til annet helsepersonale.

Vektrelaterte symptomer og hvor mye de plager deg

For hvert av de følgende spørsmålene, les listen over symptomene nedenfor, og sett et ☒ i den ene rubrikken som best beskriver svaret ditt.

a. I løpet av de siste 4 ukene, har du hatt følgende symptomer			b. Hvis Ja, i hvilken grad plaget disse symptomene deg?						
NEI	JA	SYMPTOMER	IKKE I DET HELE TATT	NESTEN IKKE	NOE	MODERAT	MYE	TEMMELIG MYE	SVÆRT MYE
☐0	☐1	Kortpustethet	☐0	☐1	☐2	☐3	☐4	☐5	☐6
☐0	☐1	Trøtthet	☐0	☐1	☐2	☐3	☐4	☐5	☐6
☐0	☐1	Søvnproblemer	☐0	☐1	☐2	☐3	☐4	☐5	☐6
☐0	☐1	Overfølsomhet for kulde	☐0	☐1	☐2	☐3	☐4	☐5	☐6
☐0	☐1	Økt tørste	☐0	☐1	☐2	☐3	☐4	☐5	☐6
☐0	☐1	Økt irritabilitet	☐0	☐1	☐2	☐3	☐4	☐5	☐6
☐0	☐1	Ryggsmerter	☐0	☐1	☐2	☐3	☐4	☐5	☐6
☐0	☐1	Hyppig vannlating	☐0	☐1	☐2	☐3	☐4	☐5	☐6
☐0	☐1	Leddsmerter (hofter, knær, osv.)	☐0	☐1	☐2	☐3	☐4	☐5	☐6
☐0	☐1	Vannopphopning i kroppen	☐0	☐1	☐2	☐3	☐4	☐5	☐6
☐0	☐1	Problemer med føttene	☐0	☐1	☐2	☐3	☐4	☐5	☐6
☐0	☐1	Overfølsomhet for varme	☐0	☐1	☐2	☐3	☐4	☐5	☐6
☐0	☐1	Snorking	☐0	☐1	☐2	☐3	☐4	☐5	☐6

(Vennligst snu arket)

(fortsatt)...

a. I løpet av de siste 4 ukene, har du hatt følgende symptomer			b. Hvis Ja, i hvilken grad plaget disse symptomene deg?						
NEI	JA	SYMPTOMER	IKKE I DET HELE TATT	NESTEN IKKE	NOE	MODERAT	MYE	TEMMELIG MYE	SVÆRT MYE
☐0	☐1	Økt apetitt	☐0	☐1	☐2	☐3	☐4	☐5	☐6
☐0	☐1	Urinlekkasje	☐0	☐1	☐2	☐3	☐4	☐5	☐6
☐0	☐1	Svimmelhet	☐0	☐1	☐2	☐3	☐4	☐5	☐6
☐0	☐1	Økt svetting	☐0	☐1	☐2	☐3	☐4	☐5	☐6
☐0	☐1	Tap av seksuell lyst	☐0	☐1	☐2	☐3	☐4	☐5	☐6
☐0	☐1	Redusert fysisk utholdenhet	☐0	☐1	☐2	☐3	☐4	☐5	☐6
☐0	☐1	Hudirritasjon/sår	☐0	☐1	☐2	☐3	☐4	☐5	☐6

Vennligst gå tilbake til spørsmålene du nettopp har besvart for å forsikre deg om at du ikke har hoppet over noen punkter

Takk for at du besvarte disse spørsmålene!